Medical Marijuana Program

165 Capitol Avenue, Room 145, Hartford, CT 06106-1630 • (860) 713-6066
E-mail: dcp.mmp@ct.gov • **Website:** www.ct.gov/dcp/mmp

Petition to Add a Medical Condition, Medical Treatment or Disease to the List of Debilitating Conditions

INSTRUCTIONS: Please complete each section of this Petition and attach all supportive documents. All attachments must include a title referencing the Section letter to which it responds. Any Petition that is not fully or properly completed will not be submitted to the Board of Physicians.

Please Note: Any individually identifiable health information contained in a Petition shall be confidential and shall not be subject to disclosure under the Freedom of Information Act, as defined in section 1-200, Connecticut General Statutes.

Section A: Petitioner's Information

Name (First, Middle, Last): Delores Edwards, Executive Director, SCDAA Southern CT/Virginia Pertillar, Executive Director CQSCC Northern		
Home Address (including Apartment or Suite #): Sickle Cell Disease Assoc. of America Southern ,545 Whalley Ave./ Citizens for Quality Sickle Cell, 370 Osgood Avenue, Unit 106		
City: SCDAA of Southern CT, New Haven/ CQSCC of Northern, New Britian	State: CT	Zip Code: 06511/06053
Telephone Number: SCDAA :(203)-385-2253/ CQSCC (860) 223-7222	E-mail Address: scdaasouthernct@sbcglobal.net / vpertillar@CQSCC.org	

Section B: Medical Condition, Medical Treatment or Disease

Please specify the medical condition, medical treatment or disease that you are seeking to add to the list of debilitating medical conditions under the Act. Be as precise as possible in identifying the condition, treatment or disease.

SICKLE CELL DISEASE

Section C: Background

Provide information evidencing the extent to which the condition, treatment or disease is generally accepted by the medical community and other experts as a valid, existing medical condition, medical treatment or disease.

- Attach a comprehensive definition from a recognized medical source.
- Attach additional pages as needed.

Section D: Negative Effects of Current Treatment

If you claim a treatment, that has been prescribed for your condition causes you to suffer (i.e. severe or chronic pain, spasticity, etc.), provide information regarding the extent to which such treatment is generally accepted by the medical community and other experts as a valid treatment for your debilitating condition.

- Attach additional pages as necessary.
- If not applicable, please indicate N/A.

Section E: Negative Effects of Condition or Treatment

Provide information regarding the extent to which the condition or the treatments thereof cause severe or chronic pain, severe nausea, spasticity or otherwise substantially limits one or more major life activities.

- Attach additional pages as necessary.

Section F: Conventional Therapies

Provide information regarding the availability of conventional medical therapies, other than those that cause suffering, to alleviate suffering caused by the condition or the treatment thereof.

- Attach additional pages as necessary.

Section G: General Evidence of Support for Medical Marijuana Treatment

Provide evidence, generally accepted among the medical community and other experts, that supports a finding that the use of marijuana alleviates suffering caused by the condition or the treatment thereof.

- Attach additional pages as necessary.

Section H: Scientific Evidence of Support for Medical Marijuana Treatment

Provide any information or studies regarding any beneficial or adverse effects from the use of marijuana in patients with the condition, treatment or disease that is the subject of the petition.

- Supporting evidence needs to be from professionally recognized sources such as peer reviewed articles or professional journals.
- Attach complete copies of any article or reference, not abstracts.

Section I: Professional Recommendations for Medical Marijuana Treatment

Attach letters in support of your petition from physicians or other licensed health care professionals knowledgeable about the condition, treatment or disease at issue.

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Section J: Submission of Petition
In the event you are unable to answer or provide the required documentation to any of the Sections above (excluding Section D); provide a detailed explanation indicating what you believe is "good cause" for not doing so. • Attach additional pages as necessary.

I hereby certify that the above information is correct and complete.	
My signature below attests that the information provided in this petition is true and that the attached documents are authentic. I formally request that the commissioner present my petition and all supporting evidence to the Board of Physicians for consideration.	
Signature: Virginia Stoltidar ▶ Delores Edwards	Date Signed: 3/25/14 3-25-14

Section B

Sickle cell disease, including, but not limited to, the common types: homozygous sickle cell disease (Hb SS), sickle cell SC disease (Hb SC), and sickle beta thalassemia (Hb S beta thal; both beta thal + and beta thal 0). Not including sickle cell trait.

For public listing purposes, we recommend the following:
Sickle cell disease (not sickle cell trait)

Section C

From the Sickle Cell Disease Awareness and Education Strategy Development Workshop Report, National Heart Lung Blood Institute, Publication No. 56-205N, April 2010: Sickle cell disease (SCD), also known as sickle cell anemia, is a serious disease in which the body makes an altered form of hemoglobin, the protein in red blood cells that carries oxygen throughout the body. This genetic alteration causes the body to produce abnormal sickle- or crescent-shaped red blood cells. Unlike normal red cells that pass smoothly through the blood vessels, sickle cells are stiff and sticky and tend to form clumps that get stuck in the blood vessels and obstruct blood flow.

The result is episodes of extreme pain ("crises"), as well as chronic damage to vital organs.

SCD is an inherited disease. People who have the disease inherit two copies of the sickle cell gene— one from each parent. If a person inherits only one copy of the sickle cell gene (from one parent), he or she will have sickle cell trait.

Sickle cell trait is different from SCD. People who have sickle cell trait do not have the disease, but they have one of the genes that cause it.

Section D

Current drug treatment of pain of sickle cell disease is incompletely effective and often involves significant side effects and risks.

Drug treatment typically involves pain medications, especially three types of medications:

- acetaminophen ("Tylenol" and others)
- NSAIDs (non-steroidal anti-inflammatory drugs)
  - ibuprofen ("Motrin" and others)
  - naproxen ("Aleve" and others)
  - and others
- opioids/narcotics
  - morphine
  - hydromorphone ("Dilaudid")
  - oxycodone ("OxyContin" and others)

Acetaminophen and NSAIDs do not provide effective relief for severe sickle cell pain. Narcotics may not provide effective relief for severe sickle cell pain. Narcotics are subject to tolerance (increasing doses required to accomplish usual effects) and dependence (discontinuation

causes illness). Narcotics cause unpleasant (for example, constipation, intense itching) and problematic (for example, impaired judgment) side effects as well as euphoric (a "high") effects that may lead to addiction (relentless, inappropriate drug use). Legal access to narcotics by prescription may facilitate illegal activities such as sale of narcotics to addicts and others. Addiction may lead to illegal activities such as theft to obtain money for the purchase of narcotics.

In addition to pain medications, other drugs of diverse types – anesthetics, anticonvulsants, antipsychotics, others – are sometimes used for the treatment of the pain of sickle cell disease, but the effects of these drugs are inconsistent and usually inadequate.

Section E

Sickle cell disease causes chronic pain. Despite current therapies including pain medications and hydroxyurea, more than half of adults with sickle cell disease report significant pain on more than half of the days of their lives (1). Almost one third of adults with sickle cell disease report significant pain almost every day of life (1). Adults with sickle cell disease average more than 12 days each year in the emergency room or hospital for pain (1).

1. Smith WR, Penberthy LT, Bovbjerg VE, McClish DK, Roberts JD, Dahman B, Aisiku IP, Levenson JL, Roseff SD. Daily assessment of pain in adults with sickle cell disease. Annals of Internal Medicine. 2008;148:94-101.

Section F

The only medicine approved specifically for the treatment of sickle cell disease is hydroxyurea. Hydroxyurea is not a pain medicine. By changing the nature of red blood cells in persons with sickle cell disease, hydroxyurea reduces painful episodes by about half. Persons with sickle cell disease who take hydroxyurea also live longer and have fewer problems in the lungs and fewer strokes. Hydroxyurea has improved outcomes for people with sickle cell disease, but it has not eliminated pain.

Section G

See Section I.

Section H

A computer assisted search of the world's medical literature through the National Institutes of Health online database (PubMed: "sickle and marijuana") conducted in March 2014 revealed

three articles about marijuana in sickle cell disease. A study from North Carolina indicated that teenagers with sickle cell disease engaged in "risky behavior", including marijuana use, less frequently than similar teenagers without sickle cell disease (1). A study from Jamaica found that marijuana use was common in young adults with sickle cell disease (2). A study from London found that almost one third of young adults with sickle cell disease had used marijuana in the previous year. The main reasons for use were to reduce pain (52%) and to induce relaxation or relieve anxiety and depression (39%) (3).

These studies suggest that many persons, especially adults, with sickle cell disease use marijuana, and some use marijuana specifically to reduce pain.

There is a limited scientific literature on the effects of marijuana on chronic pain in conditions other than sickle cell disease. This literature has been summarized with the following statement:

"There is a growing body of evidence to support the use of medical cannabis as an adjunct to or substitute for prescription opiates in the treatment of chronic pain. When used in conjunction with opiates, cannabinoids lead to a greater cumulative relief of pain, resulting in a reduction in the use of opiates (and associated side effects) by patients in a clinical setting. Additionally, cannabinoids can prevent the development of tolerance to and withdrawal from opiates, and can even rekindle opiate analgesia after a prior dosage has become ineffective" (4).

This is the primary rationale for medical marijuana for sickle cell disease: to reduce pain and to reduce the use of narcotic and other pain medications for pain.

1. Knight-Madden J, Lewis N, Hambleton IR. The prevalence of marijuana smoking in young adults with sickle cell disease: a longitudinal study. West Indian Medical Journal 2006;55:224-7.

2: Howard J, Anie KA, Holdcroft A, Korn S, Davies SC. Cannabis use in sickle cell disease: a questionnaire study. British Journal of Haematology. 2005;131:123-8.

3: Britto MT, Garrett JM, Dugliss MA, Daeschner CW Jr, Johnson CA, Leigh MW, Majure JM, Schultz WH, Konrad TR. Risky behavior in teens with cystic fibrosis or sickle cell disease: a multicenter study. Pediatrics. 1998;101:250-6.

4. Lucas PL. Cannabis as an adjunct to or substitute for opiates in the treatment of chronic pain. Journal of Psychoactive Drugs. 2012;44:125-133.

Section I

See attachment.

March 16, 2014

John D Roberts, MD
john.d.roberts@yale.edu

Dear Ms Edwards:

I welcome the opportunity to write in support of the petition of the Sickle Cell Disease Association of American Southern Connecticut Chapter to add sickle cell disease to the Connecticut Medical Marijuana Program list of debilitating conditions eligible for medical marijuana.

I have been involved in the care of persons with sickle cell disease for 20 years. In the 1990's and 2000's I was Co-Director of the Adult Sickle Cell Program at the Virginia Commonwealth University Health System. During this period I was co-author on a number of research publications on pain in sickle cell disease, one of which is cited in your petition (Smith et al, Annals of Internal Medicine 2008). In 2012 I was recruited to Yale to become the Medical Director of the Adult Sickle Cell Program of the Yale-New Haven Hospital (New Haven), where I continue to care for patients and conduct research.

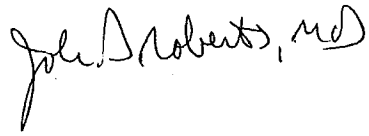
As you are aware, the hallmark of sickle cell disease is pain. Most adults with sickle cell disease experience pain most of the days of their lives. Most adults with sickle cell disease take narcotic pain medications occasionally in most years, and many adults with sickle cell disease take narcotic pain medications almost every day. Nevertheless, pain in sickle cell disease is incompletely and often poorly controlled.

Unfortunately, there is no scientific evidence concerning medical marijuana specifically in sickle cell disease. As a physician and researcher, I believe that medical marijuana might help persons with sickle cell disease in the same manner that it appears to help others with especially chronic pain. As a practitioner I know that many adults with sickle cell disease use marijuana. Many of those who are willing to discuss their use of marijuana report that it reduces their pain and decreases the amount of narcotic pain medications they take. Some adults with sickle cell disease become entangled in the criminal justice system as a consequence of their use of marijuana.

I believe that adults with sickle cell disease living in Connecticut would benefit from access to medical marijuana in terms of pain relief, reduced need for narcotic pain medications, reduced time spent in emergency rooms and hospital beds, and freedom from the threat of criminal prosecution for seeking relief from suffering.

I voice this opinion as a physician and citizen. I do not voice this opinion in any official capacity as a faculty member of Yale University or Medical Director at YNHH. This opinion does not reflect positions taken on this issue by Yale or YNHH.

Sincerely,



March 22, 2014

To Whom It May Concern:

I am submitting my opinion to the State of Connecticut to put Sickle Cell Disease on the list for Medical Marijuana use. Sickle Cell Disease should not be left out from the use of Medical Marijuana. Living your life with chronic pain is hard enough but the African American community has been long stigmatized and treated as criminals over the issues relating to the War on Drugs.

That Stigma has made it very difficult for any patient coming into a hospital during a Sickle Cell Pain Crisis from not being viewed without skepticism about the validity of their pain. It would harm our community even more if the proven benefits of Medical Marijuana were denied to patients suffering from Sickle Cell Pain.

Although Sickle Cell Disease can be found in any race of people around the world it is most common to find Sickle Cell Anemia in the Black Community. [redacted]

Medical Marijuana studies have proven over and over its benefits for Pain and Depression among many other hardships in living with Sickle Cell Disease. [redacted]

As a person living with Sickle Cell Disease I am seeking to live as pain-free as I can and if there is something out there that can ease my suffering and give me a chance at a better quality of life treatment I want to be able to ask my doctor for it.

Please add Sickle Cell Disease to the list of ailments approved for use of Medical Marijuana. I have lived 40 years with this pain so far and depression is a struggle because of Chronic Pain but never have I stepped outside of the law to try this even though I have read health and science reports on the benefits it could have in helping me cope with the challenges of living with Sickle Cell.

I have not tried something that could help me in my suffering simply because I do not wish to be seen as a criminal or the indignity of having to sneak around to buy something that can help me fight my pain. Please put Sickle Cell Disease on the list so others like me can have that choice without the stigma. Have we not suffered long enough that we must beg you to remember us in this thing? Our pain is valid too so please do not ignore our suffering.

[redacted]

Artist living with Sickle Cell Disease.

The Prevalence of Marijuana Smoking in Young Adults with Sickle Cell Disease

A Longitudinal Study

J Knight-Madden[1], N Lewis[1], IR Hambleton[1, 2]

ABSTRACT

Background: *The active ingredients of marijuana may have beneficial properties in the treatment of chronic pain and inflammation and is being used by sufferers of chronic pain and arthritis in some settings. Anecdotally, marijuana is believed by some sickle cell disease (SCD) patients to improve their health. This study aimed to determine the prevalence of marijuana smoking in the Jamaica Sickle Cell Cohort Study (JSCCS) in the years 2000 and 2004. The perception that marijuana use ameliorated the complications of SCD was also investigated.*

Methods: *All patients in the JSCCS were invited to attend an annual review, and during the 2000 and 2004 reviews, participants with homozygous sickle cell (SS) disease and sickle cell haemoglobin-C (SC) disease were asked whether they smoked marijuana, and if they smoked, whether it was used for medicinal purposes related to SCD. The authors compared smoking prevalence by gender, disease, and year of review. The association of smoking with a measure of pain frequency was also examined.*

Results: *The prevalence of marijuana smoking was higher among men and among SC participants. The proportion of either gender reporting smoking of marijuana increased in 2004 compared to 2000, and this use was not related to a simple measure of clinical severity of SCD.*

Conclusions: *Marijuana smoking is common in adults with SCD but its usage is unrelated to clinical severity of the disease.*

Prevalencia del Hábito de Fumar Marihuana en los Adultos Jóvenes con Enfermedad de Células Falciforme

Un Estudio Longitudinal

J Knight-Madden[1], N Lewis[1], IR Hambleton[1, 2]

RESUMEN

Antecedentes: *Los ingredientes de la marihuana pueden tener propiedades beneficiosas para el tratamiento del dolor e inflamación crónicos, y en algunos lugares esta planta está siendo usada por enfermos que sufren de dolor y artritis de manera crónica. De forma anecdótica, se dice que algunos pacientes de la enfermedad de células falciformes (ECF) creen que la marihuana les mejora la salud. Este estudio se propuso determinar la prevalencia del hábito de fumar marihuana en el Estudio de Cohorte Jamaicano de Células Falciformes (ECJCF) en los años 2000 y 2004. Los autores también examinaron la creencia de que el uso de la marihuana guarda relación con la percepción de que la misma mejora los casos con complicaciones por ECF.*

Métodos: *A todos los pacientes en el ECJCF, se les invita a asistir a un examen anual, y durante los exámenes de los años 2000 y 2004, a los participantes con enfermedad de célula falciforme homocigótica (SS) y con la enfermad de célula falciforme hemoglobina C (SC), se les preguntó si fumaban marihuana, y si la usaban con fines medicinales en relación con la ECF. Los autores compararon la prevalencia por género, enfermedad, y año de examen. Asimismo, examinaron la asociación del hábito de fumar marihuana con una medida de frecuencia de dolor.*

From: Sickle Cell Unit[1], Tropical Medicine Research Institute, The University of the West Indies, Kingston 7, Jamaica and Chronic Disease Research Centre[2], Tropical Medicine Research Institute, The University of the West Indies, Bridgetown, Barbados.

Correspondence: Dr J Knight-Madden, Sickle Cell Unit, Tropical Medicine Research Institute, The University of the West Indies, Kingston 7, Jamaica, West Indies. Fax: (876)927-2984, e-mail: jennifer.knightmadden@uwimona.edu.jm

Resultados. *La prevalencia del hábito de fumar marihuana fue más alta entre los hombres y entre los participantes SC. La proporción de ambos géneros que reportó hábito de fumar, aumentó en el año 2004 en comparación con el año 2000, y el uso de la marihuana no estuvo relacionado con una simple medida debida a la gravedad de la ECF.*

Conclusiones. *El hábito de fumar marihuana es común en adultos con ECF, pero su uso no guarda relación con la gravedad de la enfermedad.*

West Indian Med J 2006; 55 (4): 225

INTRODUCTION

Marijuana smoking is relatively common in Jamaica with as many as 10–15% of adult women and 37–49% of adult men having smoked marijuana at some time in their life (1, 2). The active ingredients of marijuana, in particular the cannabinoids, may have beneficial properties in the treatment of chronic pain (3–5) and inflammation (3) and, in some settings, is being used by sufferers of chronic pain (6,7) and arthritis. Marijuana may be useful in the treatment of sickle cell disease (SCD). Anecdotally, marijuana is believed by some SCD patients to improve their health. This study aimed to determine the prevalence of marijuana smoking in the Jamaica Sickle Cell Cohort Study (JSCCS) (8) in the year 2000 and whether it remained unchanged four years later. The authors also examined whether marijuana smoking among patients with SCD was related to a simple measure of painful crisis frequency and to the perception that it ameliorated complications of SCD.

SUBJECTS AND METHODS

The JSCCS incorporated all patients with SCD detected during the screening of 100 000 consecutive deliveries at the main Government Maternity Hospital from June 1973 to December 1981. These patients have been followed at the Sickle Cell Unit since birth. All JSCCS participants who have not migrated or died were asked to attend an annual review during a three week window beginning on the last Monday in January. During reviews in 2000 and 2004 homozygous SS disease (SS) and sickle cell haemoglobin-C disease (SC) participants were asked whether they had ever smoked marijuana. Additionally, in 2000, participants were asked whether they currently smoked marijuana, and in 2004 they were asked whether they had smoked marijuana in the preceding 12 months. Marijuana smokers were asked whether they used it for SCD complications and if so, the specific complications for which they used marijuana. The project was reviewed and approved by the University of the West Indies/Faculty of Medical Sciences/ University Hospital of the West Indies Ethical Committee. Written, informed consent was obtained from the subjects prior to participation in the study.

Statistics

The authors calculated the prevalence of smoking by gender and by genotype separately for each year of the study. They calculated the change in prevalence between 2000 and 2004 after adjusting for the possible confounding effects of age and gender. They also explored the association of sickle cell related pain and the prevalence of marijuana smoking using the number of independent episodes of dactylitis and uncomplicated pain crisis events requiring opioids, and occurring at least seven days after an initial event. This summary measure of pain was introduced to the logistic regression model, after adjusting for age, gender, and year of study. Stata 8 was used for all analyses (StataCorp, College Station, TX).

RESULTS

Response rate

The number of available participants fell between 2000 and 2004, mainly due to death and migration (Fig. 1). Among

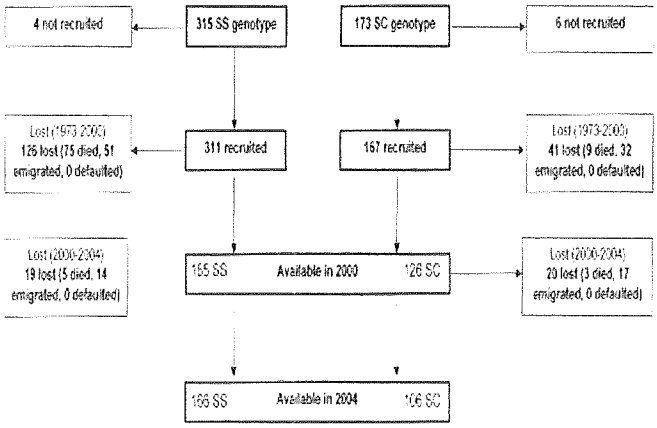


Fig. 1: Flow chart depicting the recruitment of study participants with homozygous sickle cell disease or SC disease.

available patients, the response rate in 2000 was about 90% for all genotype/sex combinations (Table). The non-responders reflected a small subgroup of chronic defaulters. The response rate in 2004 was slightly lower, especially among

Table: Number and percentage of available participants responding to questions on marijuana use in 2000 and 2004

Pattern of response	SS disease		SC disease	
	Women (%)	Men (%)	Women (%)	Men (%)
Responding in 2000	85 (94)	90 (91)	54 (89)	59 (88)
Responding in 2004	78 (88)	71 (73)	46 (77)	39 (58)
Responding in 2000 only	10	20	9	23
Responding in 2004 only	3	1	1	3
Responding in 2000 and 2004	75	70	45	36

men with haemoglobin SC disease. The increased non-response reflected participants who were usually asymptomatic and were therefore less inclined to visit the sickle cell clinic. The mean age of the study sample was 22.6 (range 18.1 to 26.6 years) in 2000 and 26.6 (range 22.1 to 30.6 years) in 2004.

Smoking prevalence

After controlling for the possible influence of age on the decision to smoke marijuana, use of smoked marijuana was higher among men and among SC participants, and the proportion of either gender reporting smoking increased in 2004 compared to 2000 (Fig. 2). In 2000, the odds of smoking were 14.7 times higher among men than women (95% CI 6.0, 35.7) and were 1.9 times higher among SC than among SS participants (95% CI 1.0, 3.5). In 2004, the odds of smoking had fallen to 6.6 times higher among men (95% confidence interval 3.7, 11.9) and were 1.5 times higher among SC participants (95% CI 0.8, 2.7). The use of marijuana had increased more among women by 2004. After adjusting for age and genotype, the odds of reporting smoking among women in 2004 *vs* 2000 were 5.4 (95% CI 2.1, 13.6), and among men were 3.8 (CI 2.1, 6.7). Of those SC participants who responded in 2000, 67% of those that did not smoke and 55% of those who did smoke were available for survey in 2004. Equivalent figures for SS participants were 84% and 66% respectively. Of those who admitted to smoking marijuana in 2004, and had attended both reviews, 58% began smoking marijuana between 2000 and 2004. Of those who reported in the 2004 survey that they had smoked marijuana, eleven (6.3%) stated that they had used marijuana because of complications of SCD. Seven patients cited painful crises while one person each identified depression, asthma and poor weight gain as the indications for marijuana use. One patient stated that marijuana was used to treat SCD but was unable to name a specific complication. There was no suggestion that smokers and non-smokers had different pain profiles: the odds of smoking did not increase with increasing pain in either 2000 (OR = 0.95, 95% CI 0.86, 1.04), or in 2004 (OR = 1.02, 95% CI 0.94, 1.11). There was little difference between smokers and non-smokers in the median number of pain events in either 2000 or 2004. By 2000 smokers and non-smokers had on average one event (interquartile range: 0–3), and by 2004 non-smokers had a single event and smokers had two events (interquartile range: 0–3 in both cases).

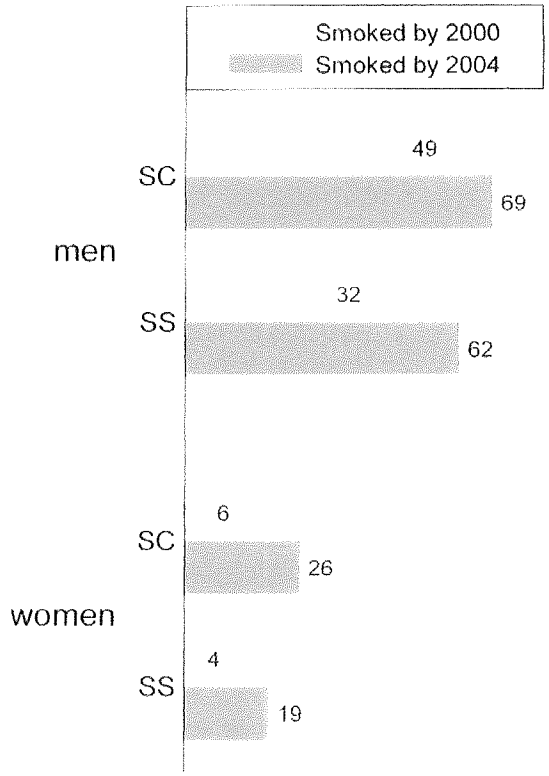


Fig. 2: Percentage of available respondents who report ever smoking marijuana by 2000 and 2004.

DISCUSSION

This study of marijuana smoking behaviour over a four-year period from 2000 to 2004 in young adults with SCD demonstrated that marijuana use was fairly common and increased between the two surveys: the prevalence of a history of smoking marijuana in women rose from 4.6% to 19.4% and in men from 38.3% to 64.6%. A population based probability sample comprised 958 Jamaicans aged 15 to 49 years and estimated the prevalence of a history of smoking marijuana to be 10% in women and 37% in men (1). In 2000, a survey of high risk health behaviours among a nationally representative sample of Jamaican adults reported that 15% of the women and 49% of the men had a history of smoking marijuana (2). The estimate reported here, particularly for men, was higher than the estimates of the prevalence of a history of smoking marijuana in the general population. This may have been due to a change in behaviour in Jamaica over time, a real difference in the prevalence of marijuana smoking in patients with SCD compared to the general population or to the difference in the ages in the reports. The possibility that this difference in reported prevalence estimates may have been due to a change in behaviour over time was supported by the reported increase in the use of marijuana over the four-year period of this study. The change in the prevalence of smoking was not due to a difference in attendance in non-smokers and smokers as 83% of non-smokers and 63% of smokers who came to the 2000 review returned in 2004. This would have tended to decrease the proportion of smokers in 2004 if the patients' behaviours were unchanged. The difference in reported prevalence estimates was unlikely to be due to the presence of SCD as few (6%) of SCD patients related their usage of marijuana to their disease, and more patients with SC disease, a milder form of the disease, used marijuana than did patients with SS disease. The higher

estimate in this study also suggests that under-reporting may not be a major source of bias.

A weakness of this study is the limitation of inquiry to smoking behaviour, as marijuana is also used in other forms, particularly as a tea. The study did not collect data to assess whether there was a possible link between amount and frequency of marijuana use (dosage), and the amelioration of complications of SCD (risk response), future studies should pursue these. The decrease in the absolute numbers of subjects in attendance between the two surveys is an almost inevitable phenomenon in long-standing cohort studies, as persons die or emigrate, but the percentage of eligible patients attending was relatively high, suggesting that this report may be representative of the sickle cell disease population nationally.

The importance of these data relate to the possible therapeutic use of marijuana in SCD. Extracts of the *Cannabis sativa* (marijuana) have been used successfully to treat a myriad of disorders. The use in the treatment of glaucoma was pioneered in Jamaica (9, 10), with the licensing of Canasol and subsequently, in combination with Timolol, Catimol, has become used internationally. Other accepted clinical indications for the use of cannabinoids include vomiting in association with cancer chemotherapy and anorexia associated with HIV wasting disease (11). Perhaps most relevant to the treatment of SCD are recently published data suggesting the usefulness of cannabinoids in the treatment of chronic pain (5), though not neuropathic pain (12). There are no data concerning the usefulness of cannabinoids in SCD but it has been suggested in the literature that trials may be considered in the near future (13). However, before introducing a drug, it is useful to determine whether individuals have previously or are currently being exposed to the drug. These data suggest that a significant proportion of SCD patients in Jamaica have been exposed to marijuana, but that the usage has not been for SCD related morbidity in most cases. Such data should be sought in any population prior to the trial or introduction of therapeutic cannabinoids.

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bjh research paper

Cannabis use in sickle cell disease: a questionnaire study

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Summary

Cannabinoids are increasingly being considered for the management of various painful conditions, and could be considered as an option for treating acute pain in sickle cell disease (SCD). The objective of this study was to determine the extent of use of cannabis in the community for pain and other symptom relief, and its side effects during self-administration in patients with SCD. Patients attending Central Middlesex Hospital in London were invited to complete a structured self-administered anonymous questionnaire. Eighty-six young adults with HbSS, HbSC and HbSβthalassaemia disease (median age 30 years) participated in the study. Results showed that 31 (36%) had used cannabis in the previous 12 months to relieve symptoms associated with SCD. The main route in all but two patients was by smoking. The main reasons for use were to reduce pain in 52%, and to induce relaxation or relieve anxiety and depression in 39%. Symptoms related to sedation and mood effects were reported in 77% of patients. The majority of patients (58%) expressed their willingness to participate in studies of cannabis as a medicine. We conclude that research in the use of cannabinoids for pain relief in SCD would be both important and acceptable to adult patients.

Keywords: sickle cell disease, pain, cannabis, cannabinoids.

Pain is one of the predominant symptoms in sickle cell disease (SCD), and is challenging in its management. This pain can be severe enough to require opioid analgesics for relief, can recur acutely at unpredicted intervals, is associated with inflammation and can become chronic, requiring regular analgesic medication with drugs, such as non-steroidal anti-inflammatory analgesics (Rees *et al*, 2003). When SCD management at home was monitored with diaries in children and adolescents, pain was frequent and many patients used single analgesics that were described as ineffective (Fuggle *et al*, 1996; Dampier *et al*, 2002). The frequency and duration of painful episodes in adults has been reported to vary widely between individuals; coping strategies influence the number of painful episodes and pain intensity (Anie *et al*, 2002), with mood being a significant component in opioid analgesia use (Anie & Steptoe, 2003).

Patients with SCD are often treated unsatisfactorily with opioids in both hospital and community settings, and this may be due to inherent problems of pain assessment or the perception of dependency on opioids (Shapiro *et al*, 1997; Maxwell *et al*, 1999). In a recent semi-structured questionnaire study of symptoms of substance dependence and abuse in patients with SCD in London, the results revealed that some coping methods could be perceived as analgesic dependence (Elander *et al*, 2003). One area of SCD pain management that has not been investigated is the use of non-proprietary preparations, such as the illicit cannabinoids found in the cannabis plant. Cannabis is commonly available in the community, and it is plausible that some patients could use it for the relief of pain associated with various medical conditions, including SCD. Nonetheless, little is known about the use of cannabis in the SCD population, and the question arises as to whether patients are using cannabis as an additional drug to improve pain relief in the community.

Cannabis contains a mixture of phytocannabinoids whose synthetic congeners have been extensively been investigated in the laboratory for their effects on pain sensation (Walker *et al*, 1999). In humans, there are few pharmaceutical preparations because of legal restrictions but a whole-plant extract (with the active cannabinoids delta-9-tetrahydrocannabinol, THC, and cannabinoid, CBD, in equal portions) has been reported to significantly improve pain relief in patients with intractable neurogenic pain (Wade *et al*, 2003). In addition, one of the active cannabinoids in cannabis, cannabinoid has been

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demonstrated in rats to have both immunosuppressive and anti-inflammatory effects in chemically induced arthritis (Malfait *et al*, 2000). The combined effects of cannabinoids as analgesics and anti-inflammatory agents suggest that they may have a beneficial therapeutic effect in SCD.

We had anecdotal evidence of cannabis used as analgesia from confidential patient accounts, however the extent of use has never been studied in a systematic way. The aims of this study were therefore to determine the extent of use of cannabis in a cross-sectional sample of adult patients, to document the medical reasons for its administration, and to explore the willingness of patients to consider cannabinoids as an alternative or complementary treatment for pain associated with SCD.

Methods

Following Local Research Ethics Committee approval we recruited adults with SCD to an anonymous questionnaire survey at the Central Middlesex Hospital (Clinic, Inpatient & Daycare Units). All adult patients were offered a patient information sheet and those who consented verbally were then entered into the study. Written consent was not taken in order to protect anonymity. Questions arising from the survey were addressed during consultations either with the medical, psychology or nursing staff in the Clinic. Patients were requested to complete the questionnaire whilst waiting or given an addressed envelope to return it to the staff.

The questionnaire was initially piloted on a small number of patients during a Clinic. The first questions were about the demographics and clinical characteristics of the patient: this was followed by questions on the use of cannabis. For those patients with a history of cannabis use we asked specific questions about their pattern of use, its effectiveness in symptom control, symptoms or side effects experienced, and whether used recreationally or medicinally. Finally, all patients were asked if they would be willing to use cannabis in the future as part of a clinical trial.

Statistical analysis was performed using GRAPHPAD PRISM (version 3.00). We compared the demographic and clinical characteristics of the patients in the study with profiles from our Sickle Cell Clinic.

Results

Demographics and clinical characteristics

Eighty-six questionnaires were completed over a period of 6 months, representing about 34% of those who could have participated. Table I shows the distribution of gender, age and haemoglobin types in this study in the 31 patients (36%) who had used cannabis and the non-users (51 patients, 64%). These figures are representative of our total clinic population, where 10% have HbSβthalassaemia, 20% HbSC, and 70% HbSS.

Table I. Demographic and clinical characteristics: users and non-users of cannabis.

	Users	Non-users	Total
Age (years): median, [interquartile] and range	29 [24–40] 18–46	30 [22–39] 15–54	30 [23–39] 15–54
Gender			
Male	13 (42)	18 (33)	31 (36)
Female	14 (45)	30 (54)	44 (51)
Unknown	4 (13)	7 (13)	11 (13)
Haemoglobin type			
HbSS	13 (42)	38 (69)	51 (59)
HbSC	8 (26)	12 (22)	20 (23)
HbSBthal	6 (19)	2 (4)	8 (9)
Unknown	4 (13)	3 (5)	7 (8)

Values within parentheses are expressed in percentage.

Severity of sickle cell disease

Sickle cell disease severity was assessed by the frequency of painful episodes in the past year in the community, and resulting hospitalisations. Pain episodes were further subdivided by disrupted or undisrupted activities. SCD severity was further determined by surrogate markers, i.e. number of complications, blood transfusions and hydroxyurea treatment (Table II). The two groups were not significantly different using the chi-square test.

Table II. Severity of SCD: users and non-users of cannabis.

	Total	Users	Non-users
Pain episodes: frequency			
Less than once a year	16 (19)	4 (13)	12 (22)
1–10 per year	31 (36)	13 (42)	18 (33)
Once a month	15 (17)	6 (19)	9 (16)
Once a week	13 (15)	4 (13)	9 (16)
Daily	4 (5)	3 (10)	1 (2)
Pain episodes: disruptive			
Less than once a year	26 (30)	5 (16)	21 (38)
1–10 per year	33 (38)	15 (48)	18 (33)
Once a month	11 (13)	3 (10)	8 (14)
Once a week	6 (7)	3 (10)	3 (5)
Daily	1 (1)	1 (3)	0 (0)
Emergency visits, median [range]	1 [0–13]	1 [0–13]	1 [0–11]
Transfusions	20 (23)	7 (23)	13 (24)
Hydroxyurea	13 (15)	4 (13)	9 (16)
SCD complications			
Strokes/transient ischaemic attacks	11 (13)	4 (13)	7 (13)
Chest syndrome	28 (33)	14 (45)	14 (25)
Priapism	3 (4)	2 (6)	1 (2)
Gall stones	23 (27)	10 (32)	13 (24)
Avascular necrosis	17 (20)	5 (16)	12 (22)
Retinopathy	2 (4)	0 (0)	2 (4)

Values within parentheses are expressed in percentage. SCD, sickle cell disease.

First and last cannabis use

Cannabis was first used at a median age of 16 years of age (range 15–26, interquartile range 15–21). Twelve respondents (39%) had used cannabis within the past week, six (19%) had used it within the past month, two (6%) within the past 6 months and eight people (26%) had not used cannabis for over a year.

Frequency, route and time of cannabis use

In the 31 respondents who reported any cannabis use, detailed questions were asked about route, frequency and time of use. The majority of patients took the cannabis by inhalation (smoking) with only three patients (10%) using the oral route (one patient used both routes). The frequency of use was reported as daily by four patients (13%), weekly by 10 patients (32%), monthly by four patients (13%) and the rest occasionally. Respondents were also asked to state how many times they used cannabis over the period of one week or one day. For the 10 responders (32%) who used cannabis at least once a week the median frequency of use was 3·5 times per week (range 1–6). For the eight responders (26%) who said they used cannabis at least once a day the median number of episodes per day was 2·5 (range 2–6).

Thirteen patients (43%) used cannabis when necessary at any time of day or night and the remainder used cannabis in the evening.

Reasons for cannabis use

Patients were asked in some detail about their reasons for cannabis use to elicit those who were using cannabis for medicinal as opposed to recreational reasons. The questions that were asked and the responses obtained are shown in Table III.

Respondents often gave several reasons for using cannabis, leading to considerable overlap between the different answers. When the answers to these questions were combined and the overlapping answers removed, 16 people (52%) used cannabis for medicinal reasons (taken to be those where cannabis was used to reduce or prevent acute or chronic pain, and to reduce the amount of painkillers taken). There was no evidence of more severe disease in these 16 patients except that avascular necrosis of the head of the femur was more common in those who used cannabis non-recreationally rather than recreationally, with four of 16 people having avascular necrosis in the medicinal group and only one of 15 in the recreational group. A further 12 people (39%) used cannabis to relax, to sleep better to reduce anxiety or depression or to improve mood. These factors may also contribute to pain management. No one in the medicinal group reported using cannabis solely to 'get high' or to improve energy levels. In the recreational group, three of five respondents (16%) who said they used cannabis to 'get high' also said they used cannabis to decrease or prevent acute or chronic pain. The other two respondents who used cannabis to 'get high' said they also used it to relax and to help them sleep. Two respondents (6%) gave no reasons why they had used cannabis, one (3%) had tried cannabis to see what it was like; none of these had used cannabis in the previous year.

Side effects from cannabis use

Beneficial or detrimental side effects from cannabis are shown in Table III.

Sleepiness and mood change were the most common side effects. Eleven of the 13 people who said sleepiness was a side effect also stated that a benefit of cannabis was that it made them sleep better, and four of the 11 people who said that mood change was a side effect of cannabis also said that cannabis improved their mood. Some of the effects of cannabis

Table III. Cannabis use, symptoms and side effects.

	Positive responses
Question	
I use cannabis when I have acute pain due to sickle cell disease	7 (23)
I use cannabis to help reduce chronic pain due to sickle cell disease	9 (29)
I use cannabis to help me relax	18 (58)
I use cannabis to stop me feeling anxious	7 (23)
I use cannabis to stop me feeling depressed	7 (23)
I use cannabis to prevent me getting pain due to sickle cell disease	3 (10)
I use cannabis to give me energy	1 (3)
I use cannabis to 'get high'	5 (16)
Cannabis reduces my pain when I have an acute crisis	8 (26)
Cannabis reduces my chronic pain	9 (29)
Cannabis reduces the frequency of my painful crises	7 (23)
Cannabis reduces the amount of painkillers I need	13 (42)
Cannabis improves my mood	11 (35)
Cannabis helps me relax	19 (61)
Cannabis helps me feel less anxious or depressed	16 (52)
Cannabis makes me sleep better	19 (61)
Cannabis makes me feel more energetic	4 (13)
Symptom or side effect	
Blurred vision	1 (3)
Dizziness	2 (6)
Poor appetite	2 (6)
Memory loss	3 (10)
Sleepiness	13 (42)
Mood change	11 (35)
Anxiety	5 (16)
None	7 (23)

Values within parentheses are expressed in percentage.

were therefore seen as either beneficial or troubling by different people and sometimes by the same person. In addition, all of the five people who said that anxiety was a side effect of cannabis also reported that cannabis made them feel less anxious when completing the questionnaire section on why they used cannabis. One person apiece reported increased appetite, inability to concentrate and paranoia.

Future use of cannabis

Fifty patients (58%) said they would be willing to participate in future studies using cannabis for the treatment of pain in SCD. This group consisted of 24 (77%) cannabis users and 26 (47%) non-users. In addition, respondents were asked if they were concerned about dependency on cannabis. Thirty-six respondents (42%) said they were concerned about this, including nine cannabis users (29%) and 27 non-users (49%). Twenty-four respondents (28%) said they would be willing to participate in studies using cannabis despite having concerns about dependency.

Discussion

The use of cannabis in this population of responders is high and clinically important given the frequent presentation of both acute and chronic pain in this sickle cell community. Severity of SCD did not appear to be a factor in determining cannabis use as there was no significant difference in severity between the group that used cannabis and the group that did not, and the median number of hospital visits was the same in both groups. Use of cannabis was more common in patients with avascular necrosis, which is associated with severe chronic pain. Increasing severity of SCD was not associated with greater cannabis use and conversely, those who used cannabis did not report markedly reduced levels of pain.

The distribution of age, gender and type of SCD found in this study is similar to that observed in our adult clinic population. The incidence of lifetime use and use in the last year are both higher in our population (36% and 27%) than in the general UK population (27% and 9%) (Ramsay *et al*, 2001). However, when our population was compared with other groups, such as those with chronic pain disorders, human immunodeficiency virus (HIV) or multiple sclerosis patients, their rates of cannabis use are very comparable (Prestage *et al*, 1996; Wesner, 1996; Dansak, 1997; Sidney, 2001; Page *et al*, 2003; Clark *et al*, 2004). For example Ware *et al* (2003) investigated 209 patients with chronic non-cancer pain; 35% reported ever using cannabis and 15% had used cannabis for pain relief. In a questionnaire study also from west London in 523 HIV-positive patients, 27% used cannabis to treat symptoms associated with HIV; in more than 90% of users pain was the main symptom (Woolridge *et al*, in press).

Sickle cell disease is a condition where there is evidence that analgesia for both acute and chronic pain is inadequate (Claster & Vichinsky, 2003). In this context of pain that is difficult to manage, cannabinoids are becoming scientifically valid analgesic agents for clinical trials. There are increasing numbers of randomised controlled trials investigating the use of different synthetic as well as plant-derived cannabinoids as analgesic agents. An early review of these studies found that there was no evidence for their efficacy in pain relief, but small numbers of patients were involved, together with different preparations with differing pharmaceutical properties (Campbell *et al*, 2001). Several small studies have shown improvement in pain control in patients with multiple sclerosis and post-operatively when cannabinoids have been used (Noyes *et al*, 1975a,b; Zajicek *et al*, 2003; Svendsen *et al*, 2004). There is evidence therefore that cannabis may have a role as an analgesic agent in patients with SCD.

Cannabis may have a further role as an adjuvant analgesic agent to allow decreased use of other analgesic agents, such as opioids. A synergistic interaction between opioids and cannabinoid systems has been described (Welch & Eads, 1999), but further work is needed to clarify the hypothesis of synergy between cannabinoids and opioids. This interaction was suggested by the findings of Holdcroft *et al* (1997) where the use of oral THC enabled a patient with 'Familial Mediterranean Fever' to decrease their intake of opioids. In the present study, 42% of cannabis users stated that they used cannabis to decrease the amounts of other pain analgesia required.

There was a high rate of side effects from cannabis use described in this study, and was reported in 78% of users. Some were beneficial, for example 11 of the 13 people who described sleepiness as a side effect of cannabis also described help with sleeping as a benefit of taking cannabis. Similarly, all of those who described anxiety as a side effect of cannabis also described cannabis as making them less anxious. These varied effects may explain why the high incidence of side effects does not seem to deter patients from taking cannabis. In addition, opioid analgesics that are used to treat acute SCD pain also have high rates of side effects that are also more life-threatening, so that patients are likely to be attracted to any methods of decreasing the dose and frequency of opioid analgesia.

This study investigated the issues of concern about the use of cannabis in clinical trials. In the community, the main route of administration is by inhalation, often with tobacco, but this cannot be encouraged in the sickle cell population because of their risk of acute and chronic chest disease. For clinical trials different preparations are being developed, such as capsules, sublingual sprays, suppositories and topical formulations. Concerns about dependency have been raised by our respondents and in the scientific community about the psychiatric side effects of cannabis, particularly in adolescence (Arseneault *et al*, 2004) and in the black community. Confounding factors in such analyses are the problems of recreational use with the potential for high doses to be used and the lack of standardised preparations. It is reassuring that a recent meta-analysis (Macleod *et al*, 2004) found no evidence for causation of mental health problems in young cannabis users, however a

possibility that such a relationship exists cannot be excluded. Also of concern in this group of patients, who have a high incidence of stroke, is the reported association between stroke and cannabis use (Mateo *et al*, 2005).

This study provides a degree of evidence that cannabis is efficacious in this group of patients in whom current treatments are inadequate. To allow them to use cannabis safely there is a need for a standardised legal preparation and clinical evidence of its efficacy. The next stage of investigation should be to develop a trial protocol to use oral cannabinoids in the treatment of acute sickle cell pain for which there is adequate support in our clinic population.

Competing interest

Anita Holdcroft is a member of the Napp Specialist Opioid Advisory Group on drug dependency.

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Risky Behavior in Teens With Cystic Fibrosis or Sickle Cell Disease: A Multicenter Study

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Risky Behavior in Teens With Cystic Fibrosis or Sickle Cell Disease: A Multicenter Study

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ABSTRACT. *Objective.* **To determine the prevalence and age of onset of common risky behaviors such as smoking and sexual activity in teens with cystic fibrosis and those with sickle cell disease and to compare their behaviors with those of adolescents in the general population.**

Design. **Survey.**

Setting. **All five major pediatric tertiary care centers in North Carolina (study participants with sickle cell disease or cystic fibrosis) and North Carolina public schools (comparison population).**

Participants. **Three hundred twenty-one adolescents with cystic fibrosis or sickle cell disease aged 12 to 19 years (mean age, 15.6 years; 49% female). Demographically matched comparison teens for each group were selected from 2760 in-school adolescents (mean age, 16.0 years; 51% female).**

Main Outcomes Measures. **Prevalence of tobacco and marijuana use, alcohol use, sexual intercourse, sexually transmitted diseases, seat belt use, weapon carrying, and age of onset of these behaviors.**

Results. **Chronically ill teens reported significantly less lifetime and current use of tobacco, marijuana, and alcohol; less sexual intercourse; less weapon carrying, less drunk driving, and more seat belt use than their peers. Nonetheless, 21% of the teens with cystic fibrosis and 30% of those with sickle cell disease had smoked; sexual intercourse was reported by 28% and 51%, respectively. Age of onset of these behaviors was frequently older for the chronically ill teens.**

Conclusion. **Teens with cystic fibrosis or sickle cell disease took more potentially damaging health risks than might be expected, although the prevalence was lower than reported by their peers. Future longitudinal studies should examine the relationships between chronic illness, physical and psychosocial maturation, and risky behavior. Screening for psychosocial issues, including risky behaviors, should be incorporated into the routine health care of chronically ill teens.** *Pediatrics* **1998;101: 250–256;** ***adolescence, chronic illness, risky behavior, cystic fibrosis, sickle cell disease.***

ABBREVIATIONS. CF, cystic fibrosis; SCD, sickle cell disease; YRBS, Youth Risk Behavior Survey.

Dramatic advances in the medical care of children with severe chronic conditions have resulted in the survival of many of them into adulthood. During the adolescent years, these teens and their families face the dual challenges of adolescent development and coping with chronic illness. Compared with physically healthy peers, chronically ill teens may experience delayed growth and pubertal maturation[1,2] and report increased concerns related to growth and body image[3,4] and to future planning.[4,5] They have been reported to have fewer close friends,[6] to have fewer friends of the opposite sex,[7] and to date less often.[5] They are also less likely to obtain a driver's license (an important marker of independence), even when their condition does not directly affect their ability to drive.[5] These maturational challenges may lead chronically ill teens to engage in risky behavior as a means of achieving developmental goals such as peer acceptance and independence. Alternatively, delayed physical and psychosocial maturation may be associated with less risky behavior than found among age-matched healthy peers.

As defined by Jessor,[8] a risk behavior is any behavior that can compromise the psychosocial aspects of successful adolescent development such as fulfillment of social roles, acquisition of essential skills, achievement of competence, and transition to young adulthood. In healthy adolescents, risk behaviors such as substance use, early sexual activity, and delinquency have been found to be highly correlated with each other, with more modest correlations found for other health-related behaviors such as safety and exercise. These patterns are hypothesized to result from the interaction of the social environment, the perceived environment, personality, biology, genetics, and other behaviors.[8]

The impact of chronic illness on these relationships is unclear. Previous studies of teens with a variety of chronic conditions found similar or lower rates of risky behaviors than those reported by healthy peers.[9–12] These studies have been marked by several

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limitations, including a focus on a small number of behaviors, the use of instruments which have not been standardized, lack of confidentiality, or small or nonrepresentative samples. The principal goal of this study was to provide a more population-based and complete picture of risky behaviors among chronically ill teens and to compare their behaviors with those of a demographically similar group of teens from the general population. To address some of the limitations of previous studies, we surveyed a geographically-based population of chronically ill teens using a standardized, reliable instrument administered in a confidential manner.

Many studies suggest that a noncategorical, rather than disease-specific, approach is most appropriate for inquiry into psychosocial issues related to chronic illness.[13–16] Rolland[14] has proposed that the psychosocial demands of a chronic illness can be categorized on the basis of time of onset, the course of the illness (progressive, stable, or relapsing/episodic), the expected outcome, and the degree of incapacitation associated with the illness. We chose to study cystic fibrosis (CF) and sickle cell disease (SCD), including hemoglobin SS, SC, and S-β-thal, because they are both congenital, with usual onset of symptoms in early childhood. Both are associated with a shortened lifespan but survival into young adulthood is increasingly common.[17,18] Although the course in CF is marked by a more gradual decline than in SCD, it also has unpredictable acute exacerbations similar to those in SCD. Both conditions are generally invisible. Some authors have suggested that those with invisible conditions are more likely to engage in risky behavior than those with more visible conditions. Finally, the two conditions share similar health care delivery models. Most patients with CF or SCD are seen at a comprehensive care center at least intermittently and thus could be identified through registries and disease-specific clinic records. Compared with national CF registry data, only five (3%) North Carolina teens with CF were not included in the tertiary care center records (FitzSimmons, personal communication, 1995). Although there is no comparable registry for SCD, it is estimated that approximately 80% of persons with SCD in North Carolina are known to one of the comprehensive SCD centers (Telfair, personal communication, 1995).

METHODS

Study Population and Recruitment

Adolescents aged 12 to 19 years with either SCD (n = 292) or CF (n = 146) were identified through registries at all five major tertiary care centers in North Carolina. All patients and their parents or guardians were contacted by mail to introduce the study. Consent was obtained and data were collected through in-person interviews during a clinic or hospital visit, or by telephone for those without visits during the 10-month study period. Of the 438 eligible teens, 35 (8%) declined to participate, 3 (1%) were excluded, (2 lacked usable data forms and 1 had undergone bone marrow transplant and no longer had SCD), and 79 (18%) could not be contacted. The study, therefore, had a total of 321 (74%) participants. Of these, 116 (36%) had CF and 205 (64%) had SCD. Teens with CF were more likely to decline participation, and teens with SCD were more likely to be interviewed by phone or not to be located. Nonparticipants were, on average, 2 months younger than participants. The gender distribution was similar.

Comparison Group

The comparison group was drawn from a sample of 2760 in-school North Carolina adolescents, selected to be representative of North Carolina youth, who completed the 1993 North Carolina Youth Risk Behavior Survey (YRBS) administered by the North Carolina Department of Public Instruction.

Matching Process

Adolescents of the same age, race, and gender as the study adolescents were randomly selected from the school sample in a 2:1 ratio. There were 6 study participants for whom no exact match existed. These were dropped from the analysis. An additional 38 study participants (mostly older black males with SCD) had only 1 demographic match. The results of preliminary bivariate analyses were not significantly different using a 1:1 versus an incomplete 2:1 match. To maximize statistical power, the 2:1 match was retained in all subsequent analyses.

Administration of Study Instruments

Extensive precautions were taken to protect study participants' confidentiality. Once informed consent was obtained from the teen and, in the case of a minor, a parent or guardian, each teen was interviewed privately in a separate room in the clinic. A research assistant unconnected with the clinic staff administered a structured interview and showed the teen how to complete the self-administered questionnaire before leaving the room. The structured interview contained questions related to health care utilization, and these data are not included in the current work. The teen completed the questionnaire and placed it in a sealed envelope and then in a sealed box. An audio-recorded version of the questionnaire was also available for teens who requested it. Because of the importance of assuring the respondents' anonymity, we made no attempt to correlate teens' reports with chart data or provider reports. The study protocol was approved by the Institutional Review Board at each of the five participating institutions. Study recruitment extended from October 1994 to August 1995.

For the comparison population, the survey was administered anonymously in a single-class period and was scored on computer-readable answer sheets. To preserve the anonymity of the school systems and students involved, data related to place of residence and school system were deleted by the Department of Public Instruction before release of the dataset to the study team. Because our study was not concerned with community or residential variables, but merely statewide norms, these data were of no consequence to the proposed analysis.

YRBS

Developed and assessed for reliability by the Centers For Disease Control and Prevention,[19] this 75-item self-administered pen and paper questionnaire assesses behaviors related to the most common adverse health outcomes among adolescents and adults. These include intentional and unintentional injury, tobacco use, alcohol and other drug use, sexual behaviors, physical inactivity and diet, and standard demographic measures. Most questions contain five to seven categories of response corresponding to increasing levels of use. The survey can be completed in 30 to 50 minutes. It has been widely used and found to be reliable.[20] A modified version of the YRBS was administered in the North Carolina schools in 1993 and included questions related to suicide and to school-based education regarding specific risk behaviors. Because teens with severe physical limitations may have less opportunity to participate in risky behaviors, additional questions were added to the chronically ill teens' survey to address self-perceived health and functional status.

Data Analysis

The main independent variable for the current analyses was presence or absence of the identified chronic illness. The main dependent variables included: seat belt and helmet use, carrying a weapon, tobacco and marijuana use, alcohol use, sexual behaviors, and suicide attempts and serious suicidal ideation. All data were analyzed using STATA 4.0 (Stata Corporation, College Station, TX). Because race and disease status are almost completely confounded for both CF and SCD, all analyses were stratified by

disease category. Univariate statistics were generated for each dependent variable. For each ill group (CF and SCD), χ^2 analyses were used to determine if there was a difference in the reported behaviors between those who were interviewed on the phone and those who completed the questionnaire in clinic. There were no significant differences, so phone and in-person responses were combined in subsequent analyses. Stratified bivariate comparisons between chronic illness status and the dependent variables were conducted using χ^2 for categorical variables and Student's t test for continuous variables. For questions related to substance abuse, the YRBS categorizes age of initiation among ever users as follows: less than 9 years, 9 to 10 years, 11 to 12 years, 13 to 14 years, 15 to 16 years, 17 or more years. Hence, the nonparametric Wilcoxin rank sum test was used to test for differences in age of initiation between the chronically ill and comparison groups. A P value of less than .05 was considered statistically significant. Odds ratios and 95% confidence intervals for the relative prevalence of behaviors between each chronically ill group and its comparison group were calculated using Cornfield's approximations. The comparison group was taken as the reference population for each analysis.

RESULTS

There were no significant differences in the age, gender, or racial distribution between each chronically ill group and its comparison group (Table 1). The teens with CF were on average, .7 years younger than the teens with SCD ($t = -2.02$, $P = .044$). The self-reported health and functional status of both chronically ill groups was high, although the teens with CF reported overall better self-perceived health and functional status than those with SCD. Of five categories (excellent, very good, good, fair, poor), 87% of those with CF and 72% of those with SCD rated their health as good or better ($\chi^2 = 10.73$, $P = .001$). Limitation of usual activity (categorized as never, now and then, sometimes, usually, always) was reported as sometimes or less frequently by 97% of those with CF and 87% of those with SCD ($\chi^2 = 10.13$, $P = .001$). There were no gender differences between the self-perceived health-status groups (ie, those with good or better health, compared with those with fair or poor health). Those reporting worse health were, on average, 8 months older than teens who rated their health as good or better. The older age of the SCD patients may partially explain their worse health status.

Substance Use

Alcohol was the most commonly reported substance used by all groups (Table 2). The teens with chronic illness were less likely to report ever using alcohol than the comparison groups. The odds ratio was smaller (indicating less relative use) for the teens with SCD than for those with CF. Age of initiation was older for both SCD ($z = 3.7$, $P < .001$) and CF ($z = 2.98$, $P = .003$) than for their comparison groups. Among those who reported ever using alcohol, chronically ill teens were less likely to report having their first drink before age 15; to have consumed alcohol in the past 30 days; or to have binged (consumed more than 5 drinks in a couple of hours) in the past 30 days. Chronically ill teens also reported less ever or regular tobacco use and less ever marijuana use. Among those who smoked cigarettes, teens with SCD had an older age of initiation ($z = 2.99$, $P = .003$) than their peers. The median age of onset was 13 to 14 years compared with 11 to 12 for peers. There was no significant difference for those with CF ($z = 1.04$, $P = .30$): Both groups had age of onset of 11 to 12 years. Among marijuana ever users, both those with CF ($z = 2.15$, $P = .03$) and SCD ($z = 2.64$, $P = .008$) had an older age of initiation than their comparison groups. Teens with CF and SCD had a median age of initiation of 13 to 14 years whereas their peers initiated marijuana use at a median age of 11 to 12 years. There were no differences in the proportion reporting cocaine or injection drug use, probably because use of these substances was uncommon in all groups.

Sexual Experience

Fewer chronically ill teens reported ever having sexual intercourse, and the age of first sexual intercourse was significantly older for teens with SCD of both genders and for boys with CF (Table 3). Only 25% of the sexually experienced teens with CF had first intercourse before the age of 15 compared with 64.4% of their sexually experienced peers (odds ratio = .18, 95% confidence interval = .08 to .45). Although early age of initiation of intercourse (<15 years) was more common among sexually experienced teens with SCD (51%), it was still less common than among their matched peers (odds ratio = .47, 95% confidence interval = .29 to .76). For the sexually experienced teens with CF, there was no difference from the comparison group in the proportion reporting risky sexual behaviors including no condom at last intercourse; no contraception (including condoms) at last intercourse; involvement in a pregnancy (ever been pregnant or partner was pregnant); or having three or more lifetime partners. The sexually experienced teens with SCD were less likely than the comparison group to report any of these risky behaviors except for involvement in a pregnancy.

TABLE 1. Participant Characteristics

	Cystic Fibrosis (n = 115)	Cystic Fibrosis Comparison (n = 230)	Sickle Cell (n = 199)	Sickle Cell Comparison (n = 360)
Age (mean ± SD)	15.5 ± 1.58	15.5 ± 1.58	16.2 ± 1.61	16.0 ± 1.66
Gender (% female)	51.3	51.3	49.8	53.9
Race (%)				
White	93.9	93.9	.5	.6
Black	3.5	3.5	99.0	98.9
Other	2.6	2.6	.5	.6
Health status ≥good (%)	87.8		71.9	
Functional activity limited ≤sometimes (%)	97.4		86.4	

TABLE 2. Substance Abuse

Category	Cystic Fibrosis (n = 115)	Cystic Fibrosis Comparison (n = 230)	Odds Ratio	95% Confidence Interval	χ^2	*P*	Sickle Cell (n = 199)	Sickle Cell Comparison (n = 360)	Odds Ratio	95% Confidence Interval	χ^2	*P*
Ever use alcohol	45.5%	63.1%	.49	.31–.78	9.31	.002	36.9%	70.1%	.25	.17–.36	56.68	<.001
Among ever alcohol users:												
Onset age <15	30.0%	52.9%	.38	.19–.76	7.73	.005	23.6%	43.9%	.39	.22–.72	9.61	.002
30-day use	36.0%	59.3%	.39	.20–.75	8.02	.005	33.3%	57.3%	.37	.22–.64	12.83	<.001
Binge* last 30 days	18.0%	35.3%	.40	.18–.89	5.15	.023	2.9%	18.4%	.13	0–.49	10.71	.001
Ever cigarette smoker	21.1%	53.3%	.20	.12–.33	40.2	<.001	30.0%	42.9%	.57	.39–.82	8.98	.003
Regular smoker (>2 days last month)	2.6%	29.6%	.06	.02–.20	34.0	<.001	6.5%	13.1%	.47	.25–.88	5.69	.017
Ever marijuana user	9.7%	29.4%	.26	.13–.51	16.5	<.001	16.8%	25.4%	.60	.38–.93	5.25	.022
Cocaine or injection drug use	2.6%	5.7%	.45	.13–1.50	1.61	.205	1.5%	4.7%	.20	.06–.62	3.84	.050

* More than 5 drinks in a couple of hours.

TABLE 3. Sexual Experience

Category	Cystic Fibrosis (n = 115)	Cystic Fibrosis Comparison (n = 230)	Odds Ratio	95% Confidence Interval	Test Result	*P*	Sickle Cell (n = 199)	Sickle Cell Comparison (n = 360)	Odds Ratio	95% Confidence Interval	Test Result	*P*
Ever sexually active	28.3%	46.4%	.46	.29–.75	$\chi^2 = 9.74$	.002	51.3%	76.4%	.33	.22–.48	$\chi^2 = 33.11$	<.001
Mean age 1st intercourse—females	15.7 yrs	14.6 yrs			$t = .027$	.237	14.8 yrs	13.9 yrs			$t = 3.97$	<.001
Mean age 1st intercourse—males	14.8 yrs	13.0 yrs			$t = -3.75$	.001	13.9 yrs	12.9 yrs			$t = -3.19$	.002
If sexually active:												
Age first intercourse <15 yrs	25%	64.4%	.18	.08–.45	$\chi^2 = 14.79$	<.001	51.0%	69.0%	.47	.29–.76	$\chi^2 = 9.72$	.002
No condom last intercourse	42.4%	46.2%	.86	.39–1.90	$\chi^2 = .14$	.71	19.2%	48.6%	.25	.14–.44	$\chi^2 = 24.7$	<.001
No contraception (including condoms) last intercourse	18.8%	13.3%	1.44	.51–4.11	$\chi^2 = .45$	.5	9.47%	22.7%	.36	.17–.75	$\chi^2 = 7.55$	.006
Ever involved in pregnancy	0%	6.7%	—	—	$\chi^2 = 2.24$	13.4	22.0%	20.4%	1.10	.625–1.95	$\chi^2 = .11$	.736
3 or more lifetime partners	46.9%	44.4%	1.10	.50–2.46	$\chi^2 = .06$	.81	54.0%	67.7%	.56	.35–.91	$\chi^2 = 5.61$	.01

TABLE 4. Safety and Injury-related Behaviors

Category	Cystic Fibrosis (n = 115)	Cystic Fibrosis Comparison (n = 230)	Odds Ratio	95% Confidence Interval	χ^2	P	Sickle Cell (n = 199)	Sickle Cell Comparison (n = 360)	Odds Ratio	95% Confidence Interval	χ^2	P
Usually or always wore seatbelt	87.8%	73.9%	2.52	1.35–4.70	8.80	.003	87.9%	66.4%	3.68	2.28–5.93	30.98	<.001
Wore helmet usually or always (if motorcycle rider)	72.0%	54.1%	2.18	.84–5.62	2.54	.11	61.1%	44.8%	1.94	.69–5.46	1.51	.218
Wore bike helmet usually or always (if bicycle rider)	8.5%	5.0%	1.76	.64–4.86	1.13	.29	6.6%	1.3%	5.40	1.52–19.10	7.45	.006
Carried weapon last 30 days	13.0%	27.8%	.39	.21–.72	9.39	.002	6.6%	24.4%	.22	.12–.40	26.96	<.001
More than one fight last year	10.4%	23.0%	.39	.20–.76	7.97	.005	16.6%	26.4%	.55	.36–.86	6.98	.008
Injured in fight in last year	0%	6.2%	—	—	1.61	.66	11.1%	10.0%	1.13	.43–2.98	4.41	.220
In car driven by someone who was drinking	12.2%	33.0%	.28	.15–.52	17.3	<.001	15.6%	34.4%	.35	.23–.54	22.76	<.001
Drank and drove	2.6%	8.9%	.29	.09–.90	4.65	.031	2.5%	10.3%	.23	.09–.57	11.05	.001
Made suicide plan	7.9%	18.3%	.38	.18–.81	6.49	.011	4.6%	15.8%	.26	.13–.53	15.12	<.001
Made suicide attempt	2.6%	8.3%	.3	.09–.97	4.07	.044	3.1%	8.0%	.37	.15–.89	5.03	.025

Safety and Injury Behavior

There was a tendency for chronically ill teens to report more health-promoting safety behaviors (Table 4), although there were statistically significant differences only for usually or always wearing a seat belt in both chronically ill groups and for usually or always wearing a bike helmet among those with SCD. Although a near majority of all groups reported wearing seat belts and motorcycle helmets, less than 10% in any group reported usually or always wearing a bike helmet. The chronically ill teens also reported less behavior which placed them at increased risk for injury. This included less weapon carrying, less fighting, less drinking and driving, and fewer suicide plans or attempts.

Chronically ill teens who reported their health status as fair or poor reported risky behaviors that were almost identical with those who rated their health as good or better. There were also no significant differences in risky behaviors between those reporting more or less functional limitation. These data were not substantially altered by adjustment for the differences in age between the groups.

DISCUSSION

We found that teens with CF or SCD reported fewer risky behaviors and more injury-prevention behaviors than their age and race-matched peers. Among ever users, the age of alcohol first use and age of marijuana first use were older for both chronically ill groups compared with their peers. For cigarette smoking and sexual intercourse, the same relationship held for those with SCD but the difference, although of the same magnitude, was not significant for those with CF. This may have been attributable to the smaller sample size for CF. Chronically ill teens with worse health status or more functional limitation reported the same frequency of risky behavior as those with less limitation, suggesting that physical inability to engage in risky behaviors did not play a significant role in the differences found between the ill and general populations. Alternatively, given the small number of teens reporting poor health or functional status, we may have lacked statistical power to detect differences between the groups.

The lower prevalence of suicidal thoughts and behaviors among the chronically ill teens was surprising, because this group has been felt to be at higher risk of depression. It is possible that this may be attributable to better access to mental health services via multidisciplinary care teams. Few teens reported using no contraception at last intercourse. Teens with SCD were significantly less likely to report no contraception (odds ratio = .36, P = .006) than their peers. Again, this difference may reflect better access to medical care.

These results are compatible with those found by other investigators. Adolescents, aged 13 to 21 years, with CF or myelomeningocele were less likely to report ever having sex,[10] whereas adult women with CF reported similar rates of sexual activity compared with healthy controls.[21] In a study of substance use among young adults with CF, rates of marijuana and

alcohol use matched national figures, whereas cigarette smoking (11% regular smokers) was less common than in the general population.[22] On the other hand, Alderman[9] compared middle adolescents (aged 14 to 17) with a variety of chronic conditions with healthy friends and found no difference in reported substance use, delinquency, ever sexual intercourse, or age at first intercourse. There was, however, a gender by chronic illness status interaction for age at first intercourse. Boys with chronic illness initiated intercourse later than their friends whereas girls with chronic illness initiated intercourse earlier than their friends.

We studied teens with CF or SCD. Both of these conditions are associated with early age of onset and delays in pubertal maturation.[1,2] We hypothesize that our finding of overall lower rates of risky behavior and older age of onset of these behaviors may be partly explained by delayed maturation. Neither our study nor those of others investigating risky behavior in chronically ill adolescents incorporated a measure of pubertal development. Thus, it is possible that the lack of difference found by Alderman[9] could be partly attributable to the heterogeneity of disease duration and severity (and consequent variable impact on puberty) found in her sample. These studies also did not explore the impact of self-esteem, family and social functioning, or environment on these behaviors. Problem behavior theory suggests that these additional variables will have strong impact on risky behavior. Further, all of these studies have been cross-sectional. Thus, although there is an association between chronic illness and lower prevalence of risky behaviors, causal pathways cannot be determined nor developmental factors explored.

There are several additional potentially important limitations to our study. First, all data were self-reported. Teenagers may overestimate behaviors that they believe to be socially desirable and underestimate those that they perceive as socially undesirable, although previous studies have found teens' self-reported substance use to be fairly accurate, as long as confidentiality was assured.[23–25] Second, participants may not be representative of the whole North Carolina CF and SCD teen population. Anecdotally, providers reported that some teens who declined to participate were those with known high risk behavior such as polysubstance abuse, truancy, and runaway. Thus, the results may underestimate the true prevalence of risky behavior among the target population. Third, although the school sample was chosen to be representative of the North Carolina population, we do not have direct measures of socioeconomic status or geographic residence. Thus, the school-based and chronically ill samples may not be similar on these unmeasured variables. It is possible that the reported differences in behavior reflect differences in socioeconomic status rather than disease-related differences. Finally, there were differences in questionnaire administration between the groups. The chronically ill teens completed the questionnaire in clinic (after a face-to-face interview) or on the telephone. The school sample completed it in the more anonymous school setting, which may have impacted reporting. We did not find any difference in reported behavior between our in-clinic and phone respondents, but we lacked statistical power to detect small differences. In adults, reporting of sensitive behaviors varied less than 3% between phone and in-person interviews.[26,27] Despite these limitations, we believe that our overall high response rate, our assurances of confidentiality, and our use of a reliable, standardized instrument lend strength to our results.

Longitudinal research is needed to more fully understand the interrelated determinants of initiation, experimentation, and continuation of risky behaviors in this population. Our findings, however, can be of immediate use to clinicians who care for these teens. Although the rates of risky behavior are lower than in the comparison population, they are higher than might be expected, particularly for sexual activity and substance use. These behaviors, which are risky for healthy teens, may pose special dangers to chronically ill teens. For example, unplanned pregnancy may be associated with both increased maternal and fetal risks. Smoking is associated with an accelerated decline in pulmonary function in those with chronic lung disease and increased risk of acute chest syndrome in those with SCD. These increased short- and long-term risks, coupled with the additional maturational challenges facing chronically ill teens, suggest that the assessment of psychosocial risk factors should be an essential component of the routine care of these patients. Previous studies indicate, however, that the primary health care needs of these youth, including anticipatory guidance and risk behavior counseling, may not receive adequate attention.[3,10,28] Clinicians, both primary care providers and subspecialists, need to incorporate screening for these issues into the routine care of adolescents with chronic illness if we are to maximize the long-term health of this population.

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