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SPECIAL ISSUE: BRIDGING THE GAP BETWEEN RESEARCH AND HEALTH POLICY-INSIGHTS FROM ROBERT WOOD JOHNSON FOUNDATION CLINICAL SCHOLARS PROGRAM

A Policy Impact Analysis of the Mandatory NCAA Sickle Cell Trait Screening Program

Beth A. Tarini, Margaret Alison Brooks, and David G. Bundy

Objective. To estimate the impact of the mandatory National Collegiate Athletic Association (NCAA) sickle cell trait (SCT) screening policy on the identification of sickle cell carriers and prevention of sudden death.

Data Source. We used NCAA reports, population-based SCT prevalence estimates, and published risks for exercise-related sudden death attributable to SCT.

Study Design. We estimated the number of sickle cell carriers identified and the number of potentially preventable sudden deaths with mandatory SCT screening of NCAA Division I athletes. We calculated the number of student-athletes with SCT using a conditional probability based upon SCT prevalence data and self-identified race/ethnicity status. We estimated sudden deaths over 10 years based on published attributable risk of exercise-related sudden death due to SCT.

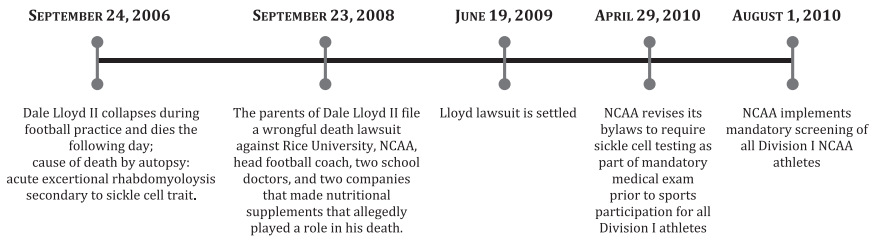
Principal Findings. We estimate that over 2,000 NCAA Division I student-athletes with SCT will be identified under this screening policy and that, without intervention, about seven NCAA Division I student-athletes would die suddenly as a complication of SCT over a 10-year period.

Conclusion. Universal sickle cell screening of NCAA Division I student-athletes will identify a substantial number of sickle cell carriers. A successful intervention could prevent about seven deaths over a decade.

Key Words. Sickle cell trait, National Collegiate Athletic Association, screening, sudden death, athletes

On August 1, 2010, the National Collegiate Athletic Association (NCAA) implemented one of the largest mandated genetic screening programs in the United States: universal sickle cell trait (SCT) screening of all Division I student-athletes (NCAA 2010b). The policy resulted from a legal settlement with the family of Dale Lloyd II, a Rice University football player, who collapsed during football practice and later died from acute exertional rhabdomyolysis attributed to SCT (Figure 1).

Figure 1: Timeline of Significant Events in the Implementation of NCAA Division I Sickle Cell Screening Program



The morbidity associated with SCT has long been debated (Sears 1978). Complications of SCT are rare and include infarction associated with hypoxia from high altitudes and renal medullary carcinoma (Tsaras et al. 2009). However, there is also concern that athletes with SCT have an elevated risk of exercise-related sudden death secondary to exertional heat illness or acute exertional rhabdomyolysis (Eichner 2010).

The NCAA’s mandatory, universal SCT screening program (NCAA Proposal No. 2009-75-B) has sparked significant debate. Endorsement of this policy from professional organizations has been mixed (College of American Pathologists 2007; National Athletic Trainers’ Association 2007; Secretary’s Advisory Committee on Heritable Disorders and Genetic Diseases in Newborns and Children’s 2010). This is due to fear that screening may lead to discrimination and confusion (Bonham, Dover, and Brody 2010), as occurred with previous community and public health sickle cell screening programs (Whitten 1973; Rutkow and Lipton 1974), as well as a paucity of evidence that screening improves health outcomes for student-athletes.

Given the scope and controversy of the screening program, we conducted a policy impact analysis (Porell and Adams 1995) to estimate the number of athletes with SCT identified and the anticipated number of exercise-related sudden deaths attributable to SCT among NCAA student-athletes.

Address correspondence to Beth A. Tarini, M.D., M.S., Assistant Professor of Pediatrics, Child Health Evaluation and Research Unit, Division of General Pediatrics, University of Michigan, 300 N. Ingalls Street, Room 6C11, Ann Arbor, MI 48109-5446; e-mail: btarini@umich.edu. Margaret Alison Brooks, M.D., M.P.H., is with the Department of Orthopedics Surgery & Pediatrics, University of Wisconsin, Madison, WI. David G. Bundy, M.D., M.P.H., is with the Department of Pediatrics, Johns Hopkins University School of Medicine, Baltimore, MD.

METHODS

Study Population: Number of Student-Athletes

We used the most recently published, publicly available NCAA participation rates (academic year 2007–2008) to estimate the number of Division I student-athletes in a 4-year cohort (e.g., all participating student-athletes in an academic year) (NCAA 2009). These data are self-reported by the 335 NCAA Division I member institutions (National Collegiate Athletic Association 2011).

The NCAA defines student-athletes as individuals who meet at least one of the following criteria by the first scheduled competition: (1) are listed as a team member, (2) practice with the varsity team and receive coaching from one or more varsity coaches, or (3) receive athletically related student aid. If a student participates in more than one sport, the NCAA counts him/her as a student-athlete participant for each sport. However, we are unaware of any publicly available NCAA statistics on the number of multisport student-athletes. To decrease the likelihood of double-counting athletes, we assumed as follows: (1) athletes who competed in cross-country also competed in track and (2) athletes who competed in indoor track also competed in outdoor track and so only included participants in outdoor track (i.e., did not include participants listed for cross country and indoor track) in our analyses.

The NCAA assigns sports to one of three categories: championship (men and women, e.g., basketball), nonchampionship (men only, e.g., rowing), and emerging (women only, e.g., rugby). The NCAA policy does not explicitly exempt student-athletes in nonchampionship and emerging sports from screening, so we included these athletes in our overall calculation of “screen-able” student-athletes. Moreover, the NCAA requires that “the [medical] examination or evaluation [which includes a sickle cell solubility test] must have been administered within six months prior to participation in any weight-training or conditioning activity” (NCAA 2010b). As all athletic activities involve weight-training or conditioning activity, student-athletes in all three NCAA sport categories meet criteria for SCT screening.

Study Population: Race/Ethnicity of Student-Athletes

Because the prevalence of SCT is increased in Black and Hispanic/Latino individuals compared to Whites (Blacks: 1/14, Hispanic/Latino: 1/183, Whites: 1/625) (Lorey, Arnopp, and Cunningham 1996), we gathered data

on the race/ethnicity distribution among all NCAA Division I student-athletes for the years 2007–2008 (NCAA 2010a). These data are self-reported by athletes. The NCAA categorizes race/ethnicity as follows: American Indian/Alaskan Native, Asian, Black/African American, Hispanic/Latino, Native Hawaiian/Pacific Islander, Other, Two or More Races, White/Non-Hispanic. “Black, Non-Hispanic” was defined as “A person having origins in any of the black racial groups of Africa (except those of Hispanic origin)”; “Hispanic/Latino” was defined as “a person of Mexican, Puerto Rican, Cuban, Central or South American or other Spanish culture or origin, regardless of race” (NCAA 2010a). We collapsed these categories as follows (Lorey, Arnopp, and Cunningham 1996): Black, Non-Hispanic; Hispanic; All Other.

Prevalence of SCT

Literature-derived estimates for the prevalence of SCT vary by ethnicity. Classically, discussion of the prevalence of SCT has focused exclusively on individuals of African ancestry. However, studies report an increased prevalence in Hispanics/Latinos compared to individuals of non-Hispanic/non-African ancestry. We used the following published point estimates for prevalence: 7 percent of blacks, 0.5 percent of Hispanics/Latinos, and 0.2 percent of whites (Lorey, Arnopp, and Cunningham 1996). We applied the 0.2 percent prevalence for whites to our “Other” race/ethnicity category.

Rates of Death for Exercise-Related Sudden Death from SCT

We identified only one study that systematically quantifies the risk of exercise-related sudden death associated with SCT. It was conducted in U.S. military recruits and categorized reasons for death into three categories: sudden unexplained death, sudden nonunexplained death (e.g., silent structural heart disease, asthma), nonsudden death (Kark et al. 1987). “Sudden death” was defined as “death due to an illness producing an irreversible critical condition within 1 hour of onset.” The authors categorized exertional heat stress, heat stroke, rhabdomyolysis, and unknown mechanism as “sudden unexplained death.” We used the death rate for “sudden unexplained death” in our analyses because it included hypothesized mechanisms (e.g., exertional heat stress, rhabdomyolysis) of exercise-related sudden death among individuals with SCT (Eichner 2010). For the risk of sudden death due to SCT in our analysis, we used the attributable death rates for sudden death among black recruits (31 deaths per 100,000 individuals) with SCT,

calculated by subtracting the death rate among black recruits with SCT (32.2 per 100,000) from the death rate among black recruits without SCT (1.2 per 100,000).

Analysis

To estimate the number of student-athletes who would suffer exercise-related sudden death due to SCT, we calculated the conditional probability of an exercise-related sudden death for student-athletes based upon the likelihood of an athlete having SCT. We assumed full compliance of all Division I member institutions with this mandatory screening policy.

Number of Athletes with SCT. First, we calculated the conditional probability of having SCT based upon ethnic group status, stratified by sport and by gender:

$$P(\text{Having SCT}) = P(\text{Race/Ethnicity}) \times P(\text{Sickle cell trait given race/ethnicity})$$

We multiplied this probability by the number of Division I student-athletes in a 4-year cohort to estimate the number of individuals who have SCT among all Division I student-athletes. We multiplied this estimate by the sensitivity of the sickle cell solubility test (98.9 percent) to determine the number of athletes with SCT identified by testing (Hicks and Hughes 1975). We then divided our total student body estimate by 4 to determine the number of athletes with SCT identified in each academic class (i.e., those identified annually).

Number of Sudden Deaths Attributable to SCT. We estimated the probability of exercise-related death from SCT conditioned upon the likelihood of having SCT, using published risk estimates (Kark et al. 1987):

$$P(\text{Death/SCT}) = P(\text{Death among individuals with SCT}) \times P(\text{Having SCT})$$

To estimate the number of expected sudden deaths in an academic year, we multiplied this probability by the number of Division I athletes participating in each sport during an academic year (i.e., 4-year cohort). We used this statistic because each year every participating athlete (newly identified SCT or already known) is at risk of sudden death from SCT. We multiplied the

number of deaths by 10 to estimate deaths over a 10-year time period, which allowed us to benchmark our model against estimates of sudden death attributable to SCT based on case reports.

Although female athletes anecdotally constitute a lower proportion of exercise-related death cases related to SCT than male athletes, we are unaware of any published data confirming this and so did not apply a gender-based differential probability of death.

Number Needed to Screen and Cost of Testing. Finally, we calculated the number needed to screen (NNS) to prevent one student-athlete death from SCT (assuming a 100 percent effective intervention). Because our data do not provide the athlete's eligibility year, we calculated the NNS over a 4-year period by assuming that $\frac{1}{4}$ of participants represented a freshman class that would only be screened once during this 4-year period.

The NCAA policy recommends that athletes be screened with a sickle cell solubility test (National Collegiate Athletic Association 2010). Positive sickle cell solubility tests must be confirmed with hemoglobin (Hb) electrophoresis. We calculated the number of student-athletes with positive sickle cell solubility tests that would undergo Hb electrophoresis by multiplying the published sensitivity estimate of 98.9 percent for sickle cell solubility testing by the number of athletes with SCT in the total athletic student body (Table 1). We did not examine the costs for false-positive results since the published specificity estimate for sickle cell solubility testing is 100 percent (Hicks and Hughes 1975). To calculate the cost of screening and confirmatory testing alone (excluding education and counseling costs), we used a range of costs for the sickle cell solubility testing (\$10–\$20) provided by different collegiate institutions (Secretary's Advisory Committee on Heritable Disorders in Newborns Meeting 2010; University of California-Berkeley 2010; Wesleyan University 2010). We used \$50 for the cost of hemoglobin electrophoresis (Chasen, Loeb-Zeitlin, and Landsberger 1999; January 22, 2010).

RESULTS

In the 2007–2008 season, 81,073 male and 63,108 female student-athletes participated in NCAA Division I sports. Football ($n = 25,658$) had the most participants for men's sports and track for women's sports ($n = 11,230$) (Appendix SA2, Supporting Information). Overall, the majority of Division I

Table 1: Estimated Number of Division I NCAA Student-Athletes with Sickle Cell Trait

	<i>Black</i>	<i>Hispanic</i>	<i>Other</i>	<i>Total</i>
Archery	0	0	0	0
Badminton	0	0	0	0
Baseball	43	3	18	64
Basketball	384	1	9	393
Bowling	9	0	0	9
Equestrian	0	0	1	2
Fencing	3	0	1	4
Field hockey	2	0	3	6
Football	833	3	26	863
Golf	13	1	9	23
Gymnastics	5	0	3	8
Ice hockey	1	0	5	6
Lacrosse	6	0	9	16
Rifle	0	0	1	1
Rowing	11	1	12	24
Rugby	0	0	0	0
Sailing	0	0	0	0
Skiing	0	0	1	1
Soccer	68	4	23	95
Softball	28	2	9	39
Squash	0	0	1	1
Swimming/diving	8	1	17	26
Sync. swimming	0	0	0	0
Team handball	0	0	0	0
Tennis	22	2	10	34
Track, outdoor	430	4	29	463
Volleyball	40	1	9	50
Water polo	1	0	2	4
Wrestling	11	1	5	16
All sports	1,918	25	204	2,147*

*This number is multiplied by 0.989 to calculate the number of athletes identified by sickle cell solubility testing = 2,123 athletes.

student-athletes self-reported a non-Black, non-Hispanic/Latino race/ethnicity (male 71.1 percent, female 80.4 percent, Appendix SA3).

Among the estimated 2,147 athletes with SCT, we estimate that 2,123 NCAA Division I student-athletes in one 4-year cohort of athletes (i.e., total athletic student body) would be identified as having SCT under this new screening policy (about 530 new students annually) (Table 1). Of these, 89 percent will self-report as Black race/ethnicity. Most student-athletes with SCT will compete in football ($n = 863$), track ($n = 463$), and basketball ($n = 393$).

In a 4-year cohort of screened NCAA student-athletes (e.g., a 4-year period with each athlete screened only once), there would be one death. Based on our model, we estimated that without intervention, about seven student-athletes with SCT would suffer exercise-related sudden death by year 10 of the screening program (Table 2).

Assuming a 100 percent effective intervention, this screening program requires that 144,181 student-athletes (e.g., a 4-year cohort of athletes) be screened to prevent one death. For each death prevented, we estimate that the cost of testing alone (i.e., without education or counseling) would range from \$1,441,810 to \$2,883,620 for sickle cell solubility testing and be about \$106,150 for hemoglobin electrophoresis confirmatory testing for those with positive sickle cell solubility tests.

DISCUSSION

The NCAA recently implemented mandatory SCT screening of all Division I student-athletes. Using publicly available data, we estimated that this policy would identify over 2,000 athletes with SCT among a 4-year cohort of student-athletes. Alongside a 100 percent effective intervention, screening could prevent the deaths of seven student athletes over a 10-year period. Our estimate approximates the number of case reports of collegiate student-athletes that have suffered exercise-related death attributed to SCT over a similar historical time interval (Eichner 2010, 2011).

A powerful motivating force behind the mandatory NCAA SCT screening policy was a wrongful death suit. As part of the settlement, the NCAA agreed to require that all Division I athletes be screened for SCT before sports participation (Lanier Law Firm 2009). Previously, the NCAA had recommended, but not required, that member institutions screen athletes for SCT (NCAA 2008b); compliance from member institutions had been variable (Clarke et al. 2006).

The NCAA SCT screening policy yields interesting comparisons to the controversy surrounding cardiovascular screening of college athletes to prevent sudden death. The NCAA does not currently recommend universal ECG screening for student athletes despite the fact that cardiovascular conditions underlie more than half of medically related sudden deaths among college athletes (Harmon et al. 2011) and data exist to support the notion that ECG screening may reduce the incidence of cardiovascular sudden death (Corrado et al. 1998). Admittedly, issues remain to be resolved (e.g., nontrivial

Table 2: Estimated Exercise-Related Deaths from Sick Cell Trait in NCAA Division I Student-Athletes That Would Be Prevented over 10 Years

	<i>Deaths</i>
Archery	0.0
Badminton	0.0
Baseball	0.2
Basketball	1.2
Bowling	0.0
Equestrian	0.0
Fencing	0.0
Field hockey	0.0
Football	2.7
Golf	0.1
Gymnastics	0.0
Ice hockey	0.0
Lacrosse	0.0
Rifle	0.0
Rowing	0.1
Rugby	0.0
Sailing	0.0
Skiing	0.0
Soccer	0.2
Softball	0.1
Squash	0.0
Swimming/diving	0.1
Sync. swimming	0.0
Team handball	0.0
Tennis	0.1
Track, outdoor	1.4
Volleyball	0.2
Water polo	0.0
Wrestling	0.1
All sports	6.5

incidence and consequence of false-positive test results, uncertainty that screening would lead to a reduction in the number of deaths from cardiovascular causes). However, a reasonable argument could be made that the evidence base supporting an NCAA recommendation for universal ECG screening appears more robust than that for universal SCT screening.

The relationship between exercise-related death and SCT has long been debated. While ample evidence suggests that SCT has not limited the competitiveness of professional football players (Murphy 1973), national track champions (Pearson 1989; Bile et al. 1998), or elite sprinters (Marlin et al. 2005), case reports of exercise-related sudden death in athletes with SCT at all levels

of sports (e.g., high school through professional) suggest a compelling pattern. Exercise-related sudden deaths attributed to SCT tend to occur in male athletes, early in training (often on the first day), and during conditioning workouts. They tend to be associated with high levels of exertion, such as short, maximum-effort drills/testing, such as those frequently used in football, a sport in which numerous sudden deaths have been attributed to SCT (Eichner 2010, 2011). Environmental conditions, such as the heat and hydration status of the player, also play an important role. These data suggest that a gene–environment interaction promotes the initiation of acidosis and rhabdomyolysis that triggers sickling and creates a rapid downward spiral from which recovery is difficult (Eichner 2010).

The “treatment” for the athlete with SCT is proactive prevention that focuses on appropriate preseason and in-season conditioning. To this end, the NCAA recommends a number of precautionary strategies for athletes with SCT (Figure 2). There is evidence that preventive hydration and temperature-monitoring strategies are effective. A 1970s study of U.S. military recruits found an increase in unexplained sudden death among individuals with SCT, compared to those without (Kark et al. 1987). However, unlike the NCAA, the U.S. military implemented universal *intervention* rather than *screening*. In an experimental study of universal precautionary measures (e.g., aggressive hydration, temperature monitoring) *without* a priori knowledge of recruits’ SCT status, the military was able to prevent all subsequent sudden death in recruits with SCT (Kark et al. 1999). This universal intervention program may yield positive spillover effects to other life-threatening conditions unrelated to SCT (e.g., exertional heat stroke) that benefit *all* athletes, not just those with SCT.

Of course, successful screening programs depend upon effective and accessible interventions. It is unclear how the NCAA enforces compliance with its “safe conditioning” recommendation and there does not seem to be a strong mandate for intervention. The NCAA informs athletes and member institutions that “Student-athletes with SCT should be knowledgeable of these precautions and institutions should provide an environment in which these precautions may be activated” (2008a). However, the ongoing challenge of compliance with sports-related concussion guidelines highlights the power of the “pressure to play” after an individual is identified as being at risk for sports-related injury. Such pressure to perform and dismiss early symptoms is likely no different for student-athletes with SCT. For example, in 2008 a collegiate football player died during a football-conditioning workout despite the fact that he and the athletic staff were aware that he had SCT. He had reportedly

Figure 2: NCAA Recommended Precautions for Student-Athletes with Sick Cell Trait (NCAA 2010b)

- Set their own pace.
- Engage in a slow and gradual pre-season conditioning regimen to be prepared for sports-specific performance testing and the rigors of competitive intercollegiate athletics.
- Build up slowly while training (e.g., paced progressions).
- Use adequate rest and recovery between repetitions, especially during “gassers” and intense station or “mat” drills.
- Not be urged to perform all-out exertion of any kind beyond 2 to 3 minutes without a breather.
- Be excused from performance tests such as serial sprints or timed mile runs, especially if these are not normal sport activities.
- Stop activity immediately upon struggling or experiencing symptoms such as muscle pain, abnormal weakness, undue fatigue, or breathlessness.
- Stay well hydrated at all times, especially in hot and humid conditions.
- Maintain proper asthma management.
- Refrain from extreme exercise during acute illness, if feeling ill, or while experiencing a fever.
- Access supplemental oxygen at altitude as needed.
- Seek prompt medical care when experiencing unusual distress.

tested positive for SCT *twice* in 2007 (Fainaru-Wada 2008)—highlighting that screening can lead to a false sense of security if an effective intervention is not enforced.

Although the NCAA policy may be based more litigation based, rather than evidence based, it has real-life implications for the athletes and schools forced to comply with it. First, there are economic costs to the member institutions that must carry out the education and testing. Second, there is the potential for discrimination toward athletes both during and after their collegiate

athletic careers. While precautions should be taken, athletic programs should not exclude these athletes or discourage them from being competitive, but rather, according to the NCAA “enable them to thrive in their sport” (2008a). Similarly, when some of these student-athletes transition to professional athletics, coaches and athletic directors should ensure that athletes with SCT do not suffer employment discrimination due to their genetic status. The history of screening for SCT is littered with stories of misinformation, stigma, and unjustified exclusion from activities and professions (Levin 1958; Whitten 1973).

Our policy analysis has limitations. First, NCAA Division II and III athletes are also at risk for exercise-related sudden death due to SCT. While they comprise a significant proportion (61 percent) of collegiate athletes, we did not include them in our formal analyses because the current NCAA SCT screening policy is limited to Division I athletes. Using identical methods, we calculated that 1,210 Division II and 675 Division III athletes would be identified as having SCT (Appendices SA4 and SA5). Assuming an effective intervention, it will take about 3 years to prevent a death in Division II and over 4 years in Division III (data not shown). Second, student-athletes that participate in multiple Division I sports could have been double-counted, leading to an overestimate of individuals with SCT. We have attempted to account for this by only including athletes who participated in outdoor track (i.e., not indoor track or cross country). Although some multisport athletes probably remain in our model, their effect on our results should be small and lead to only a slight overestimation of sudden deaths. Third, testing costs are based on publicly available costs provided to student-athletes by institutions and probably vary across institutions. However, we feel that the testing cost estimates used in our analysis are reasonable and illustrate that while the costs of individual tests are inexpensive, the cost of testing across all student-athletes is not trivial. Finally, we assumed that Division I college student-athletes do not have a greater or lesser proportion of individuals with SCT compared to the general population. Based on previous studies of elite athletes, we have no reason to believe that we have overestimated the prevalence of SCT in this population (Murphy 1973; Bile et al. 1998). In fact, a study of elite sprinters found an overrepresentation of individuals with SCT among title winners (Marlin et al. 2005).

Despite these limitations, we feel that our analysis has important implications for policy makers. First, it provides data about the scope and impact of a policy whose implementation was driven by litigation rather than evidence. Additional studies could explore the scope of screening-related harms, the costs of screening, and the effectiveness of and compliance with interventions. A successful screening program consists of both identification and action—in

this case, rigorous compliance with conditioning precautions. Evidence of this intervention's effectiveness is sorely needed, because *interventions*, not screening tests, save lives. For this screening policy to be successful, testing must be only the first step in the NCAA's overall strategy. However, the question still remains whether SCT screening is a necessary step to prevent exercise-related sudden death in student-athletes.

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SUPPORTING INFORMATION

Additional supporting information may be found in the online version of this article:

Appendix SA1: Author Matrix.

Appendix SA2: Number of NCAA Division I Athletes in 2007–2008, by Sport and Gender.

Appendix SA3: Race/Ethnicity Distribution for NCAA Division I Athletes, 2007–2008, by Sport and Gender (%).

Appendix SA4: Estimated Number of Division II NCAA Student-Athletes Who Have Sickle Cell Trait.

Appendix SA5: Estimated Number of Division III NCAA Student-Athletes Who Have Sickle Cell Trait.

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