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SEASONAL VARIATION IN SLIPPED CAPITAL FEMORAL EPIPHYSIS: NEW FINDINGS USING A NATIONAL CHILDREN'S HOSPITAL DATA BASE

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ABSTRACT

Background: Slipped capital femoral epiphysis (SCFE) demonstrates seasonal variation in certain latitudes but not others. Is such variation influenced by temperature differences, sunlight exposure and subsequent vitamin D production or other climate variables? It was the purpose of this study to further investigate the seasonal variation in month of presentation for SCFE.

Methods: Data for this study originated from the Pediatric Hospital Information System (PHIS) for all children with a diagnosis of SCFE from January 1, 2004 through December 31, 2014. From this database the patient's gender, ethnicity, hospital location, and month of presentation was determined. Only those patients treated primarily for SCFE were included. Geographic and climate data (latitude, average annual temperature, precipitation, climate type [Köppen-Geiger and Liss], horticultural plant zone hardiness, and sunlight exposure) for each of the 49 PHIS hospitals was determined. Seasonal variation was analyzed using cosinor analysis. A $p < 0.05$ was considered statistically significant.

Results: There were 10,350 cases of SCFE with an overall peak presentation in mid August. For those living at a latitude of > 35° N there was single peak, a less prominent double peak for those 31-35° N, and no variation for those < 31° N. As the average annual temperature increased there was less seasonal variability. Humid, temperate and cold winter climates demonstrated seasonal variation while other climate types did not. Those living in areas having < 2500 hours of sunlight per year demonstrated seasonal variation. Further, areas having a photovoltaic solar production potential <5.0 kWh/m^2/day also demonstrated seasonal variation.

Conclusions: We discovered new seasonal variation findings regarding SCFE. These are a double peak pattern for those between 31-35°N latitude; less variability as the average annual temperature increases; and sunlight exposure correlates with seasonal variability. Potential explanations are a rachitic state due to seasonal variation in vitamin D production, and seasonal variation in physeal growth and strength. These new findings will require further investigation.

Level of Evidence: III

Slipped capital femoral epiphysis (SCFE) often demonstrates seasonal variation in both presentation to the clinician and onset of the disorder (1-4). Many questions have arisen from these studies, especially differences between varying degrees of latitude (3, 5) – how can that be explained? Does such variation represent temperature differences, sunlight exposure with different amounts vitamin D production (6), or other even more esoteric climactic variables? With the advent of large national data bases, seasonal variation in SCFE, if it does exist, can be more fully explored. It was the purpose of this study to further investigate the seasonal variation in SCFE.

MATERIALS AND METHODS

Data for this study was obtained from the Pediatric Hospital Information System (PHIS), an administrative database that contains inpatient, emergency department, ambulatory surgery and observation encounter-level data from over 45 not-for-profit, tertiary care pediatric hospitals in the United States which are affiliated with the Children's Hospital Association (Overland Park, KS). This data base is being increasingly used in pediatric studies with over 500 published peer reviewed manuscripts as of July 2017 (personal communication, Mr. Shawn Reid, Children's Hospital Association analytics). Data quality and reliability are assured through a joint effort between the Children's Hospital Association and participating hospitals. Portions of the data submission and data quality processes for the PHIS database are managed by Truven Health Analytics (Ann Arbor, MI). Data is de-identified and subjected to a number of reliability and validity checks before included in the database. Although primarily a financial administrative database, there is large amount of clinical information such as demographics, episodes of care, and treatment(s) rendered. The study was determined to be exempt by our local Institutional Review Board.

The data base was queried for those children with a primary ICD 9 diagnosis of 732.2 (nontraumatic slipped upper femoral epiphysis) from January 1, 2004 through December 31, 2014. The following information was obtained: gender and ethnicity, hospital, medical record number, date of birth and admission, and treatment rendered. Treatment for non SCFE related issues was excluded (e.g. emergency room visits for asthma, etc.). We only included those patients treated with internal fixation *in-situ*, closed reduction and internal fixation, and open reduction and internal fixation. Procedures such as osteotomy, osteoplasty, etc. were excluded as they were likely reconstructive procedures and most likely not the first SCFE treatment. Cases due to complications associated with SCFE (e.g. fracture, avascular necrosis, complications with internal fixation, infection, etc.) were excluded as well as endocrine or renal associated SCFEs.

The month of presentation for the SCFE was defined as the initial month that each particular patient was entered into the data base for the initial SCFE treatment episode. When there was more than one month per patient, each treatment was reviewed to ensure that the subsequent procedures were not for reconstructive procedures or those related to a complication. If not, then the 2nd presentation was considered to be the opposite hip in a child with sequential presentations of bilateral SCFE. Thus sequential bilateral SCFEs are counted twice, while any child having a simultaneous bilateral SCFE presentation is counted only once. The PHIS does not record the duration of symptoms making it impossible to determine the month of onset.

Geographic and climate data were collected for each of the 49 PHIS hospital cities (Supplemental Table 1) from the National Oceanic and Atmospheric Administration (7). We collected several measures of climate severity and sunlight exposure. These were 1) horticultural plant zone hardiness, 2) climate type (8, 9), 3) cumulative sun exposure in hours per year (10), and 4) potential solar electrical production from photovoltaic resources (11) (Supplemental Figures 1-3).

The horticultural plant zone hardiness scale (12) is one proxy for climate severity. The zones vary from 1 to 13 and represent the average annual minimum temperature with 1 being the coldest; it can be accessed at http://planthardiness.ars.usda.gov. Climate type was categorized using both the well known Köppen-Geiger classification (8) and the newer Liss classification (9). The Köppen-Geiger classification is composed of 3 letters. The 1st letter is a description of the main climate, the 2nd the amount of precipitation, and the 3rd the temperature, for 31 different climate types; it can be accessed at http://koeppen-geiger.vu-wien.ac.at. Liss et al. (9) condensed these 31 types into eight types involving a four letter scheme. The 1st two letters represent the winter and the 2nd two the summer; the 1st and 3rd letters are upper case and designate the climate type (C = cold, H = hot, T = temperate) while the 2nd and 4th are lower case and designate the amount of precipitation (a = arid, d = moderately dry, and w = wet). For example, TwCd is a climate with a temperate, wet winter and a cold, moderately dry summer.

Sunlight exposure for each PHIS hospital was quantified using two different methods. The first was hours of sunlight exposure each year (10). The second more exact method used photovoltaic solar resource, a measure of the ability to transform sunlight energy into other products, such as electricity or vitamin D. Each city was grouped by 0.5 $kWh/m^2/day$ increments, using National Renewal Energy Laboratory data, and can be accessed at http://www.nrel.gov/gis/solar.html. (11).

Statistical Analysis

Univariate and bivariate analyses were used to determine the mean and standard deviation for continuous variables and frequencies/percentages for categorical variables. Temporal variation was analyzed using cosinor analysis (13) which represents a mathematical best fit of the data to a curve defined by the equation $F(t) = M + A\cos(\omega t + \phi)$, where M = the mean level (termed mesor), A = the amplitude of the cosine curve, ϕ = acrophase (phase angle of the maximum value), ω = the frequency (which for monthly analysis is 360°/12 = 30°), and t = time (which in this case is each month). The overall p and r^2 values represent a rhythmic pattern described by the cosinor equation for M, A, and ϕ. The data was analyzed for the entire period of 12 months, as well as decreasing increments of 1 month. A best fit may not be a period of 12 months, but a different time span (e.g. 6 months periodicity). Cosinor analyses were performed with ChronoLab 3.0™ software (Acknowledgement). All other analyses were performed using Systat 10™ software (Chicago, Illinois, 2000). A $p < 0.05$ was considered statistically significant for all analyses.

RESULTS

A total of 13,168 procedures were performed in 11,058 unique SCFE patients. There were 10,350 treatment episodes appropriate for seasonal analysis. Overall, there was a peak presentation in mid August (Figure 1) which did not differ by gender, Black/White ethnicity, or unilateral/bilateral nature. There were significant single peaks for those > 35° N latitude, a less prominent double peak for those 31-35° N latitude, and no variation for those < 31° N latitude (Figure 2). As the average annual temperature (Supplemental Table 2) or plant zone increased (Supplemental Figure 4) there was less seasonal variability. Seasonal variation was absent in arid locations but present in wetter climates. Thus latitude, ambient temperature, and precipitation correlate with SCFE month of presentation.

Analyses using the Köppen-Geiger and Liss classification schemes (Supplemental Table 3) demonstrated that single peaks occurred in temperate and cold winter climates that are relatively humid; warm arid or fully hot and humid climates demonstrated minimal variation. Sunlight exposure was also associated with seasonal variation in SCFE (Supplemental Table 4). Those living in areas having < 2500 hours of sunlight per year demonstrated seasonal variation (Supplemental Figure 5A) as well as those where the solar voltaic production was < 5.0 kWh/m^2/day (Supplemental Figure 5B).

DISCUSSION

Seasonal variation in SCFE was first described in 1971 (14). There was a July to November peak in boys, which was attributed to increased physical activity from playing football. In girls, the peak range was one month earlier. Subsequent studies have confirmed a seasonal variation in SCFE, with peak presentations in the late summer or early autumn (1-4). A USA wide study noted variations both north and south of the 40°N latitude; 57.4% of those north occurred April through September, while 57.3% of those south occurred October through March (15).

We must first acknowledge potential weaknesses of this study. There is always the possibility that certain data was wrongly entered into the data base, such as the wrong diagnosis or treatment. Also, it is possible that not all cases of SCFE each year for each hospital were entered. The magnitude of such a potential error is difficult to know. However, failure to enter a case would most likely be a random event, and thus equally distributed over an entire year which would not create any biased error regarding seasonal variation. Even if only 50% of the cases were entered (eg 10,350 of 20,700), such a 50% sample would have, at a 95% confidence level, a margin of error of only 0.68% (see Supplemental Materials for further discussion). Next, for any reader of this study working at one of the hospital locations described in Supplemental Table 1, must understand that the number of cases of SCFE at their institution over the time span of this study (2004 through 2014) may not be the actual number shown in Supplemental Table 1. This is due to two issues. The first is that not all hospitals became PHIS members in 2004. Many of the hospitals became PHIS members distributed at different points along the time line from 2004 – 2014, which would appear to demonstrate a conflicting numbers of cases. The second is that we excluded secondary and reconstructive cases; a hospital having a high volume of quaternary referrals for osteotomies or other reconstructive procedures will have a larger number of SCFE cases than noted in this study. Another potential weakness is that we may have excluded some patients with bilateral disease at the time a second, sequential SCFE presented. However, the percentage of sequential bilaterality was 20.1% (2,083 in 10,350), very similar to other figures of bilaterality. Another potential criticism is that the latitude of where the patient lives is markedly different than the treating hospital. That could clearly be present if the treatment was referral to a quaternary care center for advanced hip preservation surgery; however, any potential reconstructive cases were excluded. It is unlikely that large number of patients traveled enough distance to change the latitude grouping by 5°, the latitude strata used in this study, for their initial care. Finally, the data used to determine plant hardiness zones, climate classification, and solar energy potential does not exactly span the same years as this study, but these are the most recent data available. Since we averaged the results over 11 years, and since the climate graphs also used averaging methods, we propose that those graphs are very applicable to our data.

The major strength of this study is that it is the largest series to date (10,350 cases) reviewing seasonal variation of SCFE, more than double the previous largest United States series of 4,690 (3). Also, the data in this study is actual patient data, not a 20% sampling of discharge data from the Nationwide Inpatient Sample used by Brown (3).

No mathematical modeling of biologic processes is perfect. A perfect fit of any data would demonstrate an r^2 of 1.00. When reviewing the statistically significant cosinor models in this study, the reader should understand that a $p < 0.05$, although significant, may show considerable variability as demonstrated by the r^2 value. The goal of this study was not to fit the data to a highly accurate, complex mathematical model, but rather to demonstrate trends that might show further insight into the etiology of SCFE. This caveat must be remembered when reviewing our results. Further details are discussed in the Supplemental Materials.

With these caveats in mind, in this study, we confirmed many of the previous findings and discovered new ones regarding SCFE seasonal variation. For those living north of the 35° N latitude, there was significant seasonal variation, with a peak presentation mid to late August. In the more southern latitudes, there was a double peak pattern for those between 31-35°N latitude and no variation for those < 31°N latitude. This is the first that a double peak has been described in the USA. Such a peak was noted in a nation-wide study in Japan. The latitude of Tokyo, the most populous city in Japan, is 36°N, very similar to the 31-35°N in this study.

This is the first study to explore correlations between SCFE seasonal variation and climate. As the average annual temperature increases, there is less variability. Seasonal variation was absent in arid locations. There were single peaks in the relatively humid, temperate and cold winter climates. Warm arid climates or fully hot and humid climates demonstrated no significant variation. Finally, the magnitude of sunlight exposure was associated with seasonal differences. Those living in cities with < 2500 hours of sunlight exposure per year or photovoltaic solar production potential < 5.0 $kWh/m^2/day$ demonstrated seasonal variation; those having more sunlight exposure demonstrated no seasonal variation.

There are many potential explanations for these findings. An intriguing one is that SCFE may represent a rachitic state, which has been postulated by several authors (3, 5, 6). Such seasonal variation could be explained by differences in vitamin D production and levels at different times of the year. It is well known that vitamin D levels in children vary by time of the year (16). The high prevalence of vitamin D insufficiency/deficiency in children and adolescents (16) is higher in Blacks than in Caucasians (17) and in obese compared to non obese children (18). These findings nicely fit the known demographics of SCFE which is more common in obese (19) and Black (15, 19) children. Vitamin D deficient rats demonstrate extensive disorganization in the growth plate (20). In such rats the chondrocyte columns in the hypertrophic and proliferative zones are aligned in varying directions and not parallel to the axis of growth, impacting its mechanical properties to shear stress. This histopathologic disarray is also seen in SCFE.

Few studies address vitamin D levels in SCFE. A study of 20 consecutive children from Los Angeles with SCFE and found no vitamin D deficiency, regardless of obesity status. The majority of the children studied were

Hispanic (17 of 20), but the time of year when the vitamin D levels were collected was not given (21). In Vellore, India, all 15 children with SCFE had significantly lower vitamin D levels than the controls (22). In Southampton, England (23) 85% of children with SCFE were vitamin D deficient.

Another intriguing hypothesis is the relationship between seasonal variation in SCFE and seasonal variation in height and weight growth velocity. In general, maximum height velocity occurs in the spring and summer, and maximum weight velocity in the fall and winter. The physis becomes weaker with increasing physeal thickness. Does a maximum height gain in the spring and summer, with the theoretical increase in physeal height during maximum height growth, result in SCFE that then presents slightly thereafter? The correlation between physeal height and SCFE has been described in humans, with acceleration in skeletal growth just before the slip occurs (24).

The bimodal pattern noted in the more southern, warmer latitudes is intriguing. Some authors have postulated increased physical activity at the peak onset of SCFE (14). Such activity is difficult to quantify, especially in a review using this type of a data base. However, the bimodal pattern seen in the southern, warmer latitudes could be explained by more physical activity in the spring and autumn when the weather is more amenable to outdoor activity compared to the very hot summer. This bimodal pattern can not be explained by seasonal variations in vitamin D, as studies from more southern latitudes note that vitamin D levels are higher in the summer and lower in the winter like that seen in more northern latitudes.

We could not analyze the month of onset of the SCFE, as the duration of symptoms was not known. Other studies addressing seasonal variation of SCFE using national databases have the same handicap of not knowing the duration of symptoms (3, 15). Previous studies that determined month of onset (1, 5, 25) subtracted the symptom duration from the month of presentation. The average duration of symptoms was approximately four months in all three studies. This time interval in diagnosis of SCFE has not changed for decades and ranges from two to 6.5 months. If we assume that the average symptom duration is 3 to 4 months (some will be greater, and others less, but on average this 3 to 4 months is likely a reasonable estimate), then the overall month of onset would be around May, similar to an older study (1).

In conclusion, this is the first study to investigate other climate influences on seasonal variation in SCFE. It has corroborated many of the other studies demonstrating a seasonal variation in SCFE, yet has also given new insights into the possible effects of latitude and climate variables on seasonal variation of SCFE. The synthesis and explanations of these new findings will require further investigation.

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LEGENDS FOR FIGURES

Figure 1: The percentage of all SCFEs by month of presentation. Cosinor analysis demonstrated an excellent fit using a 12 month periodicity with the equation percentage of SCFEs = 8.338 + 0.961(cos(30t-15)-226), where t = 1 is January, 2 = February, 11 = November, 12 = December. This was statistically significant ($r^2 = 0.58$, p = 0.021). The peak was August 17 (arrow). The data are represented by the bars and the best fit cosinor curve by the bold black line.

Figure 2: Differences in SCFE seasonal variation by latitude.
A: Percentage of SCFEs by month of presentation in northern latitudes. Cosinor analysis demonstrated an excellent fit using a 12 month periodicity for both those between 35-40°N latitude (black squares and solid line) and >40°N latitude (open triangles and dashed line). The equation for the 35-40°N latitude group is percentage of SCFEs = 8.338 + 1.029(cos(30t-15)-225) ($r^2 = 0.55$, p = 0.028) - peak August 16 (solid arrow); for the >40°N latitude group is percentage of SCFEs = 8.339 + 1.337(cos(30t-15)-235) ($r^2 = 0.74$, p = 0.002) - peak August 26 (dashed arrow).

B: Percentage of SCFEs by month of presentation in the southern latitudes. Cosinor analysis demonstrated an excellent fit using a 5 month periodicity for those between 31-35°N latitude (black triangles and solid line) with the equation percentage of SCFEs = 8.441 + 0.856(cos(72t-36)-226) ($r^2 = 0.52$, p = 0.036). Since the periodicity is 5 months, the December 31 and January 1 points are not exactly equal. The peaks were April 6 and September 5 (solid arrows). For those living < 31°N latitude (open squares and dashed line) there was no significant cosinor fit.

Figure 1

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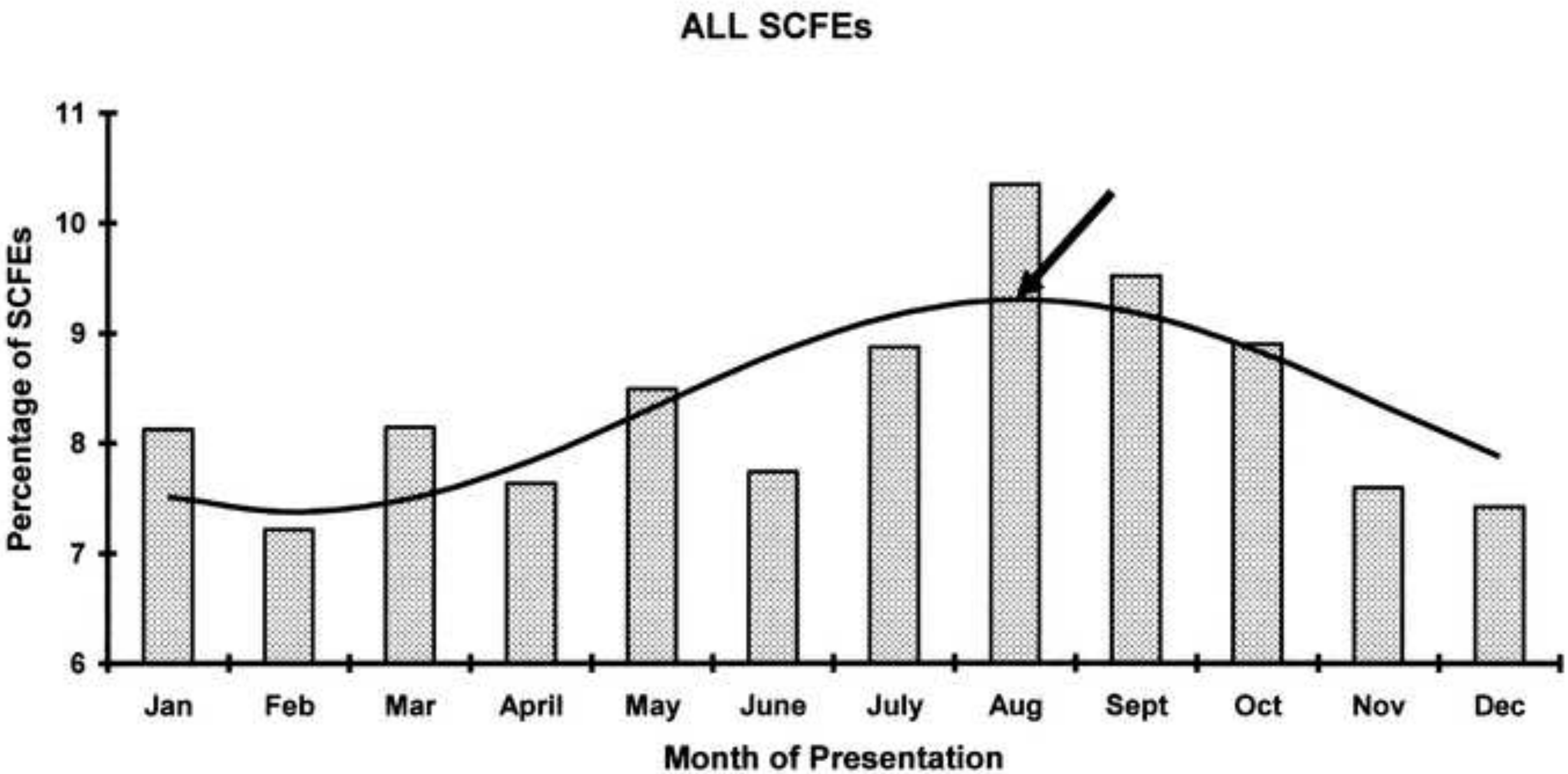

Figure 1

Figure 2A

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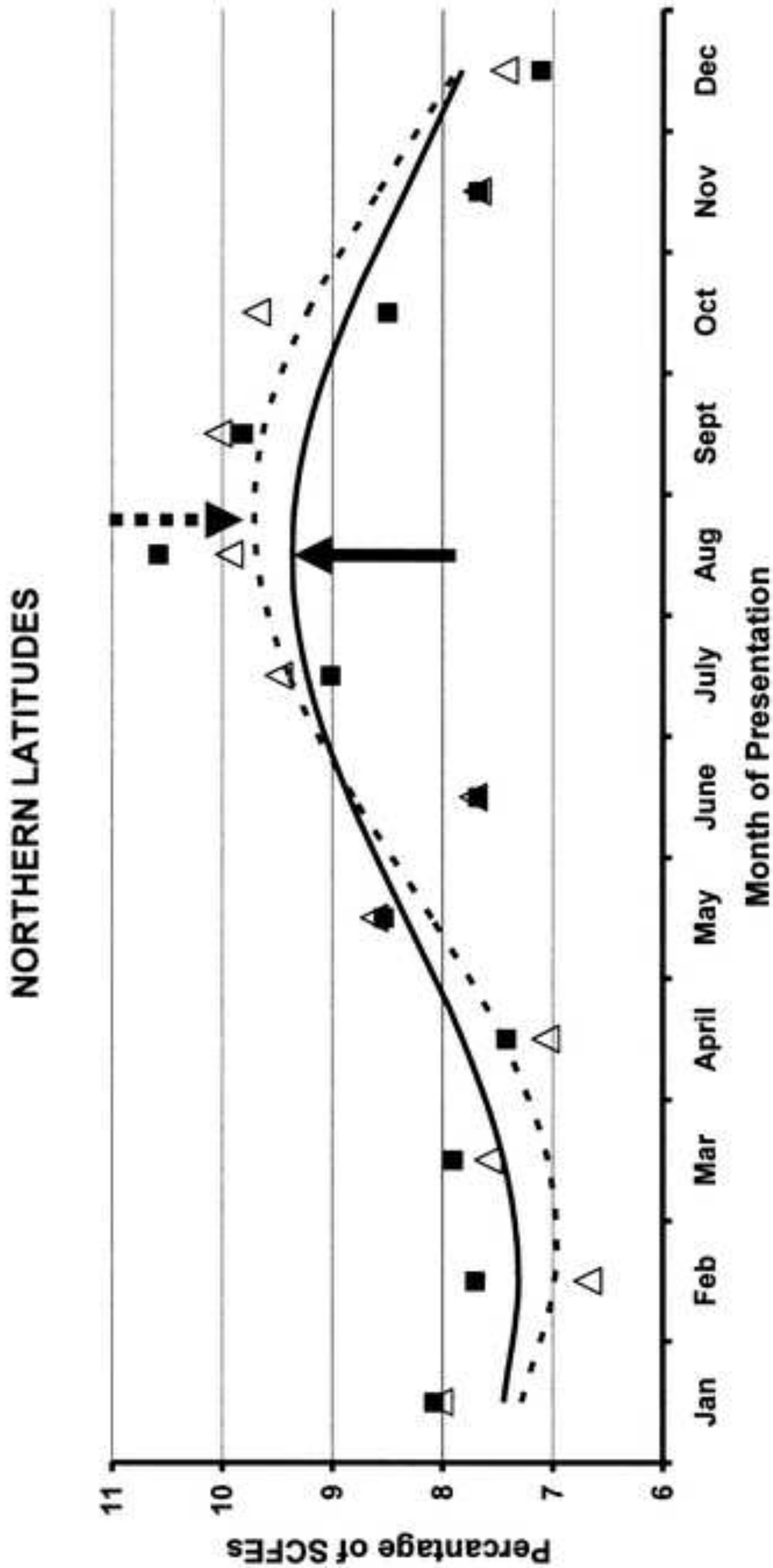

Figure 2A

Figure 2B

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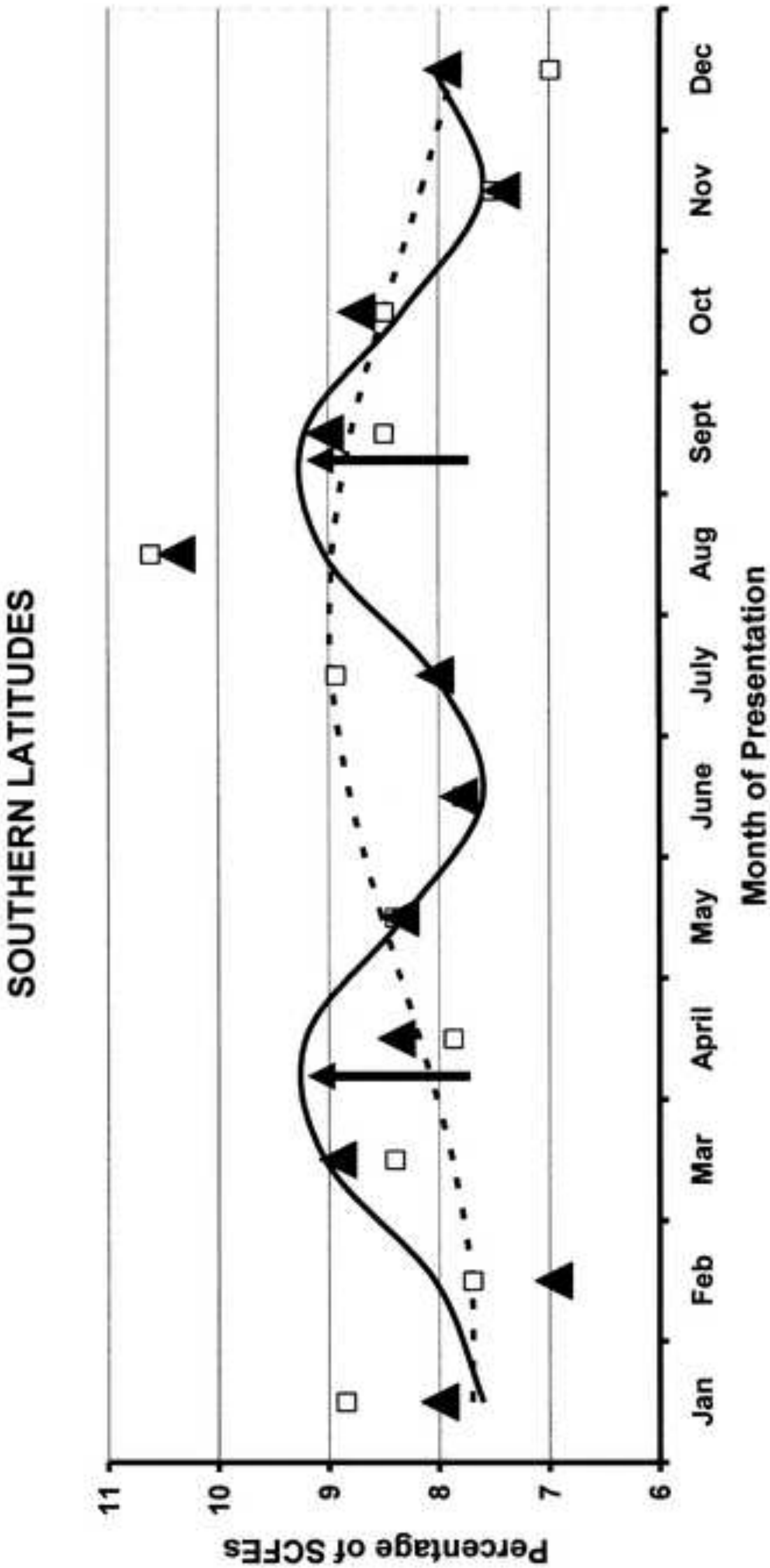

Figure 2B

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