Jennifer Latella

Exercises

Questions 1 and 2 refer to the following article (see abstract and table below):
Lucas A et al. Randomized Trial of Nutrient-Enriched Formula Versus Standard Formula for Postdischarge Preterm Infants. Lucas A et al. Pediatrics 2001, 108:703-711.

ABSTRACT. *Objectives.* Preterm infants are frequently discharged from the hospital growth retarded and show reduced growth throughout childhood. In a large efficacy and safety trial, we tested the hypothesis that nutritional intervention in the first 9 months postterm would reverse postdischarge growth deficits and improve neurodevelopment without adverse safety outcomes.

Participants and intervention. Two hundred eighty-four infants (mean gestation: 30.9 weeks) were studied; 229 were randomly assigned a protein, energy, mineral, and micronutrient-enriched postdischarge formula (PDF; $N = 113$) or standard term formula (TF; $N = 116$) from discharge (mean 36.5 weeks' postmenstrual age). A reference group ($N = 65$) was breastfed until at least 6 weeks' postterm.

Outcome measures. Anthropometry was performed at 6 weeks and 3, 6, 9, and 18 months. Development was measured at 9 months (Knobloch, Passamanick, and Sherrard's developmental screening inventory) and 18 months (Bayley Scales of Infant Development II; primary outcome) postterm.

Results. At 9 months, compared with the TF group, those fed PDF were heavier (difference 370 g; 95% confidence interval [CI]: 84–660) and longer (difference 1.1 cm; 95% CI: 0.3–1.9); the difference in length persisted at 18 months (difference 0.82 cm; 95% CI: −0.04–1.7). There was no effect on head circumference. The effect of diet was greatest in males; at 9 months length deficit with TF was 1.5cm (95% CI: 0.3–2.7), and this remained at 18 months (1.5cm [95% CI: 0.3–2.7]). There was no significant difference in developmental scores at 9 or 18 months, although PDF infants had a 2.8 (−1.3–6.8) point advantage in Bayley motor score scales. At 6 weeks' postterm, exclusively breastfed infants were already 513 g (95% CI: 310–715) lighter and 1.6cm (95% CI: 0.8–2.3) shorter than the PDF group, and they remained smaller up to 9 months' postterm.

Conclusions. 1) Improving postdischarge nutrition in the first 9 months may "reset" subsequent growth—at least until 18 months for body length. We intend to follow-up the children at older ages. The observed efficacy of PDF was not associated with adverse safety outcomes. 2) We cannot reject the hypothesis that postdischarge nutrition benefits motor development and this requires additional study. 3) Our data raise the possibility that breastfed postdischarge preterm infants may require nutritional supplementation, currently under investigation. *Pediatrics* 2001;108:703–711; *preterm infant, growth, neurodevelopment, randomized trial, diet.*

ABBREVIATIONS. PDF, postdischarge formula; TF, term formula; MUAC, mid-upper arm circumference; SD, standard deviation; CI, confidence interval.

TABLE 4. Postdischarge Growth in Boys and Girls According to Randomized Diet

	Boys		Girls	
	PDF $n = 58$	TF $n = 55$	PDF $n = 55$	TF $n = 61$
9 months				
Weight (kg)	8.83 (1.13)	8.26 (0.95)*	7.89 (0.85)	7.75 (0.91)
Length (cm)	71.9 (3.3)	70.4 (2.5)*	69.8 (2.7)	69.2 (2.2)
Occipto-frontal head circumference (cm)	46.1 (1.9)	46.2 (1.3)	45.1 (1.4)	45.1 (1.4)
18 months				
Weight (kg)	10.77 (1.34)	10.51 (0.97)	9.64 (0.95)	9.72 (1.23)
Length (cm)	81.7 (3.4)	80.2 (2.6)*	79.5 (2.9)	79.3 (2.6)
Occipto-frontal head circumference (cm)	48.2 (1.8)	48.3 (1.6)	46.9 (1.5)	47.2 (1.5)

Results are mean (SD).
* $P < .05$

1. Perform an appropriate statistical test to compare the postdischarge formula vs. the standard term formula in boys in terms of weight at 9 months. Remember to state the null and alternate hypotheses. Draw a conclusion from your result.

2. Find a 95% confidence interval for the difference in length at 18 months between PDF-fed and TF-fed boys.

Questions 3 to 6 refer to the following article (see abstract and tables below):
Metzl JD et al. Creatine Use Among Young Athletes. Pediatrics 2001, 108(2): 421-425.

ABSTRACT. *Objective.* Creatine is a nutritional supplement that is purported to be a safe ergogenic aid in adults. Although as many as 28% of collegiate athletes admit taking creatine, there is little information about creatine use or potential health risk in children and adolescents. Although the use of creatine is not recommended in people less than 18 years of age, numerous anecdotal reports indicate widespread use in young athletes. The purpose of this study was to determine the frequency, risk factors, and demographics of creatine use among middle and high school student athletes.

Methods. Before their annual sports preparticipation physical examinations, middle and high school athletes aged 10 to 18 in Westchester County, a suburb north of New York City, were surveyed in a confidential manner. Information was collected regarding school grade, gender, specific sport participation, and creatine use.

Results. Overall, 62 of 1103 participants (5.6%) admitted taking creatine. Creatine use was reported in every grade, from 6 to 12. Forty-four percent of grade 12 athletes surveyed reported using creatine. Creatine use was significantly more common ($P < .001$) among boys (53/604, 8.8%) than girls (9/492, 1.8%). Although creatine was taken by participants in every sport, use was significantly more common among football players, wrestlers, hockey players, gymnasts, and lacrosse players ($P < .001$ for all). The most common reasons cited for taking creatine were enhanced performance (74.2% of users) and improved appearance (61.3%), and the most common reason cited for not taking creatine was safety (45.7% of nonusers).

Conclusions. Despite current recommendations against use in adolescents less than 18 years old, creatine is being used by middle and high school athletes at all grade levels. The prevalence in grades 11 and 12 approaches levels reported among collegiate athletes. Until the safety of creatine can be established in adolescents, the use of this product should be discouraged. *Pediatrics* 2001;108:421–425; *creatine, nutritional supplements, ergogenic aids, adolescent sports medicine, preparticipation examination.*

ABBREVIATIONS. FDA, US Food and Drug Administration; ATP, adenosine triphosphate; ADP, adenosine diphosphate.

TABLE 1. Creatine Use by School and Sex

School	Type	Grade Level	Socioeconomic Status	Number of Creatine Users/Number of Subjects (%)	Number of Female Users/Number of Females (%)	Number of Male Users/Number of Males (%)
A	Public	Middle	M/U	5/260 (1.9)	2/101 (2.0)	3/159 (1.9)
B	Public	High	M/U	25/325 (7.7)	2/146 (1.4)	23/175 (13.1)
C	Private	High	M	10/108 (9.3)	2/56 (3.6)	8/52 (15.4)
D	Public	High	M	11/162 (6.8)	0/74 (0)	11/88 (12.5)
E	Public	Middle	M	11/248 (4.4)	3/115 (2.6)	8/130 (6.2)
Total				62/1103 (5.6)	9/492 (1.8)	53/604 (8.8)

M/U indicates middle and upper class; M, middle class.

TABLE 2. Creatine Use by Grade

Grade	Number of Participants	Users	% Use
6	69	2	2.9
7	240	5	2.1
8	195	9	4.6
9	233	7	3.0
10	173	8	4.6
11	158	19	12.0
12	27	12	44.4
11 and 12	185	31	16.8

TABLE 3. Creatine Use by Sport of Participation

Sport	Number of Users/Total Number of Participants (%)
Gymnastics	4/11 (36.4)
Hockey	8/40 (20.0)
Wrestling	8/56 (14.3)
Football	24/179 (13.4)
Lacrosse	18/143 (12.6)
Cheerleading	3/40 (7.5)
Swimming	4/61 (6.6)
Skiing	3/52 (5.8)
Tennis	4/91 (4.4)
Baseball	7/162 (4.3)
Soccer	10/256 (3.9)
Field hockey	2/117 (1.7)
Track	4/280 (1.4)
Weight training	51/527 (9.7)

3. The article states that 62 of the 1103 participants (5.6%) admitted taking creatine. Give a 90% confidence interval for this and explain what it means.

4. The article states: "Creatine use was significantly more common ($p<0.001$) among boys (53/604, 8%) than girls (9/492, 1.8%). Verify the p value by an appropriate test.

5. Refer to table 3. Suppose all 40 hockey players (and no one else) attended a hockey meeting after class. Then at this gathering, 10 were picked randomly to participate in a nationwide hockey event. What is the probability that at least half of these chosen students use creatine?

6. Refer to table 1. Compare schools C (private) and D (public) in terms of numbers of students using creatine by using the X^2 test. State the null and alternate hypotheses and draw a conclusion.

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Jennifer Latella

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Exercises

Answers

1. For boys at 9 months (weight):

H_0 : $\mu_1 = \mu_2$

H_a : $\mu_1 \neq \mu_2$

① PDF $\bar{x}_1 = 8.83$ $s_1 = 1.13$

③ TF $\bar{x}_2 = 8.26$ $s_2 = 0.95$

Performing a t-test for independent samples (unpaired):

df = 54 (as per Moore and McCabe, smaller of $n_1 - 1$ and $n_2 - 1$)

$$t = \frac{8.83 - 8.26}{\sqrt{\frac{1.13^2}{58} + \frac{0.95^2}{55}}} = \frac{0.57}{0.196} = 2.91$$

Using table D, using df 50, we get:

(2-sided)

$0.005 < p < 0.01$ So at 0.01 level of significance, we can reject the null hypothesis of no difference in the means for weight at 9 months (boys).

Could also subtract weight at discharge (probably small < 1 kg and would improve precision)

2. 95% CI for difference in length (18 months) for boys:

$$(81.7 - 80.2) \pm t_{54} \sqrt{\frac{3.4^2}{58} + \frac{2.6^2}{55}} \qquad df = 54$$

$$1.5 \pm 2.009 \times 0.568$$

using df 50 in table D → $(0.36, 2.64)$

3. $\hat{p} = 0.056$ use creatine (assume all users admit to their use)

$$SE_{\hat{p}} = \sqrt{\frac{0.056(0.944)}{1103}}$$

$$= 0.00692$$

$$0.056 \pm \overbrace{1.645 \times 0.00692}^{0.0114}$$

$(0.045, 0.067)$ → We are 90% confident that the true proportion of creatine users among middle and high school students lies between 4.5% and 6.7%.

4a

4. Let's use a z test for 2 proportions:

$H_0: p_B = p_G$

$H_a: p_B \neq p_G$ (→ Here, we could have used a one-sided H_a thinking boys take part in activities requiring ↑ muscle strength and thus more likely to use creatine.)

$$z = \frac{0.088 - 0.019}{0.0140} = 5$$

$$SE_{D_p} = \sqrt{0.0566(0.9434)\left(\frac{1}{604} + \frac{1}{492}\right)} = 0.0140$$

$$\hat{p} = \frac{53 + 9}{604 + 492} = 0.0566$$

$P < 0.0004$ (2-sided) table C

So we can reject H_0 at $\alpha = 0.001$; creatine use rates are indeed significantly different between boys and girls.

From Hypergeometric Function in Excel

P(0)	.076
1	.264
2	.347
3	.222
4	.075
5	.013
6	.001
7	.000
8	.000

5. Using the binomial distribution, we have

$B(10, 0.20)$

Using table C:

$$P(X \geq 5) = 0.0264 + 0.0055 + 0.0008 + 0.0001 = 0.0328$$

or 3%

6. Using χ^2 test, we must set up a 2×2 table:

Observed

		Creatine use: yes	no	
School	C	10	98	108
	D	11	151	162
		21	249	270

We must set up table of expected values:

Expected

		Creatine use: yes	no	
School	C	8.4	99.6	108
	D	12.6	149.4	162
		21	249	270

H_0: There is no association between creatine use and students attending either school C or D.

H_a: There is indeed an association between creatine use and attending school C or D.

Then $\chi^2 = \sum \frac{(|O-E| - 0.5)^2}{E}$ df = 1

$= 0.144 + 0.012 + 0.096 + 0.008$

$= 0.26$ → very small

so we cannot reject the null hypothesis of no association between use and school attended.