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Low-calorie Sweeteners: Disturbing the Energy Balance Equation in Adolescents?

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Abstract

Objective—To investigate the relationship between LCS, energy intake, and weight in United States youth.

Methods—Data were collected from individuals aged 2 to 19 years, who participated in NHANES in 2009–2010 (n=3,296), 2011–2012 (n=3,139), and 2013–2014 (n=3,034). Logistic regression, unadjusted and adjusted for age, sex, race/ethnicity, income, energy intake, and physical activity, was used to estimate the odds of obesity in LCS consumers vs. non-consumers, overall, and across product categories (foods vs. beverages) and socio-demographic subgroups.

Results—Among adolescents, odds of obesity were 55% and 70% higher in LCS beverage consumers compared to non-consumers, in unadjusted and adjusted models, respectively. Energy intakes did not differ based on LCS consumption. In contrast, associations between LCS consumption and obesity risk were not statistically significant among children (2–11 years old), except in boys and those who self-identified as Hispanic.

Conclusions—LCS consumption is associated with increased odds of obesity among adolescents. This relationship is strikingly independent of total energy intake. While findings should be interpreted cautiously due to limitations of self-report dietary intake and the cross-sectional nature of this analysis, our observational analysis supports the need to investigate mechanisms by which LCS may influence body weight, independently of changes in energy intake.

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Introduction

Low-calorie sweetener (LCS) consumption is increasingly prevalent among youth[1]. Beverages are the predominant contributors to LCS intake in children, although LCS are also found widely in foods, condiments, and sweetener packets[1]. While LCS offer a lower-calorie alternative to added sugars, their role in weight management and metabolic health is unclear[2].

Epidemiologic studies report positive associations between LCS and body weight in children and adults[3]. However, little is known about whether LCS consumption correlates with energy intake, especially in youth. In adults, LCS consumers have higher discretionary calorie intake[4], purchase more snack foods, and consume more calories[5], compared to sugar-sweetened beverage (SSB) consumers. A recent analysis also reported that overweight and obese adults who consume LCS beverages have higher calorie intake compared to similar weight individuals who consume SSB[6]. Despite the growing body of epidemiologic literature connecting LCS intake to higher body weight in adults[7], causality cannot be inferred from observational analyses, and the majority of randomized controlled trials in adults demonstrate that LCS may be a useful tool for modest weight loss in the context of intensive lifestyle interventions[8,9]. Meanwhile, population-level relationships between LCS consumption, energy intake, and obesity in youth have not been evaluated. We investigated this relationship in youth, using data from three cycles (2009–2014) of the National Health and Nutrition Examination Survey (NHANES).

Methods

Data source

NHANES is a continuous, cross-sectional study of the US population, with data released in 2-year cycles. NHANES sampling and data collection methods are described elsewhere[17]. The current analyses used data collected from individuals aged 2 to 19 years, who participated in NHANES 2009–2010, 2011–2012, and 2013–2014, providing a sample of 9,469 individuals. NHANES response rates were ≥75%, for the age-groups studied, in all three survey cycles[10]. Demographic and anthropometric were collected, categorized, and analyzed as detailed previously[1]. Consistent with prior analyses[1], those with missing weight (n=177) or implausible energy intake (n=31) were excluded, providing a final sample of 9,261. Participants with missing data for any characteristic were excluded only from the subgroup comparison for which information was missing. Because assessment of physical activity in NHANES (described below) differs for younger children (2–11 years) and adolescents (12–19 years), all analyses were conducted separately for children (2–5 years, 6–11 years) and adolescents (12–19 years).

LCS Consumption

LCS use was also identified and categorized in accordance with our prior publications[1,11]. Briefly, food and beverage items containing LCSs reported during the 24-hour recalls were identified using food descriptions provided in the Food and Nutrient Database for Dietary Studies (FNDDS) version 5.0[21] and version 11–12[22], in NHANES 2009–2010 and

NHANES 2011–2014, respectively. Food codes containing the terms "diet," "dietetic," "low-calorie," "no sugar added", "light", "sugar-free", "sugar substitute," "low-calorie sweetener," or "no-calorie sweetener" were extracted. After confirming that food codes extracted did indeed reflect the presence of LCS (e.g. a food such as light mayonnaise does not contain LCS despite being labeled 'light') using publicly available ingredient information, each code was then categorized as an LCS beverage, or LCS food. Any participant who completed one (n= 1,299) or both (n= 8,170) dietary recalls was included in the analysis. Children who reported consuming ≥1 food or beverage containing LCSs during at least one of their two dietary recalls were defined as LCS consumers.

Obesity

Body mass index percentile was then calculated based on measured height and weight and weight status subgroups (underweight, normal weight, overweight, or obese) were determined using standard cut-offs. Obesity was defined as BMI at or above the sex-specific 95th percentile of BMI for age, based on the 2000 CDC growth charts[12,13].

Physical Activity

For children (2–11y), physical activity was assessed as number of days physically active at least 60 min per week. This was assessed based on the question, 'During the past 7 days, on how many days was participant physically active for a total of at least 60 minutes per day?' For adolescents (12–19), physical activity was assessed as MET-min of moderate and vigorous activity per week, which was derived using NHANES recommended MET score. This was assessed based on the question, 'In a typical week, on how many days do you do moderate or vigorous-intensity sports, fitness or recreational activities, and how much time {do you/does SP} spend doing vigorous-intensity sports, fitness or recreational activities on a typical day?

Covariates

Covariates included the participant's age (categorized as child or adolescent), sex, socioeconomic status (coded as low, middle, or high, determined using tertiles of family income to poverty ratio), and self-reported race-ethnicity (coded as non-Hispanic white, non-Hispanic black, Hispanic, or other), energy intake, and physical activity.

Statistical Analysis

SAS 9.4 (SAS Institute, 2013) was used to account for the complex sampling design. Sample weights were used to generate national-level estimates of consumption. Differences in sociodemographic characteristics across weight categories were examined by F-test. Logistic regression, unadjusted and adjusted for age, sex, race/ethnicity, income, energy intake, and physical activity, was used to estimate the obesity odds in LCS consumers vs. non-consumers. All p-values were 2-sided and $p< 0.05$ was considered statistically significant. Values are presented as odds ratios (OR) with 95% confidence intervals (CI) or percentages, as appropriate.

Results

Sociodemographic characteristics by weight status and reported LCS consumption are presented in Table 1 and Table 2, respectively. Odds ratios of obesity overall and by product category are shown in Table 3. LCS packet use was not separately analyzed, due to low prevalence of LCS packet use in youth.

Among adolescents, obesity odds were 55% and 70% higher in LCS beverage consumers compared to non-consumers, in unadjusted and adjusted models, respectively. This pattern was observed across sex and income strata. In contrast, LCS food consumption was not associated with obesity odds and daily energy intakes did not differ based on LCS consumption (Table 2). Associations between LCS consumption and obesity were not consistently observed in children 2–11 years, except in males and Hispanics, before and after adjustment. Energy intakes did not differ with LCS consumption in any subgroup (Supplemental Table).

Discussion

LCS beverage consumption is associated with obesity in US adolescents, even after adjustment for relevant covariates, including energy intake. This finding is also supported by recent data in adults, where BMI was consistently higher with increasing diet beverage consumption, despite similar reported daily energy intakes[14]. While the observed associations do not imply causation, these results underscore the need to investigate mechanisms by which LCS may independently influence weight. LCS have been shown to upregulate adipogenesis and inhibit lipolysis *in vitro,* and alter gut microbiota in rodents[15]. Augmentation of insulin is reported in humans[16] and is particularly relevant for adolescents, given the physiological insulin resistance of puberty[17].

The lack of an association observed between consumption of LCS foods and obesity risk across sociodemographic subgroups is noteworthy. While likely explained by the low prevalence of LCS foods among children and adolescents, it is also possible that LCS foods are used differently in the diet compared to LCS beverages and thus may be associated with different dietary patterns or lifestyle habits.

Lack of consistent associations in younger children is likely multifactorial. Since obesity is much more prevalent in children above the age of 6 years compared to 2–5 year olds[18], combining data from young and school-aged children may be misleading. In addition, if LCS are determined to be causally related to the development of obesity, it may occur gradually and will thus be observable only in older children. Also, LCS consumption is much more common in adolescents and thus, greater exposure may be necessary to observe an association[1]. Heightened susceptibility to LCS's effects on insulin secretion (e.g. insulin resistance of puberty) may also be necessary[17].

Limitations of the current investigation include analysis of self-reported dietary recall data, which is subject to systematic bias and susceptible to misreporting of energy intake, specifically among individuals with obesity[19,20]. In addition, as the observational nature of our study is not sufficient to establish causation, the observed effects may be in part explained by reverse causality and residual confounding. Furthermore, it is not possible to distinguish between different LCS using NHANES dietary data and potential misclassification of consumers is possible with self-report dietary assessment.

Conclusion

Taken together, our observational findings emphasize the need to determine whether chronic LCS ingestion is causally related to the development of obesity. It is also important to consider race/ethnicity, gender, age, and other factors when evaluating potential effects of LCS on body weight, as heterogeneity in associations was observed across socio-demographic subgroups.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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What is already known about this subject?

- Low-calorie sweetener use has increased markedly in children and adolescents over the past decade
- Low-calorie sweetener use is associated with obesity and metabolic disease in adults.
- Low-calorie sweetener use is associated with higher energy intake in adults but this has not been examined in children

What does your study add?

- Adolescents who consume beverages containing low-calorie sweeteners have significantly higher odds of obesity, even when adjusted for total calorie intake.
- Daily energy intakes do not differ with low-calorie sweetener consumption in children or adolescents.
- Our findings support the need to elucidate the physiologic mechanisms through which low-calorie sweetener may paradoxically increase body weight, independently of changes in energy intake.

Table 1

Characteristics of Child and Adolescent NHANES 2009–2014 Participants[a] Overall and Stratified by Weight Status Categories[b]

CHILDREN (2–11 YEARS)						
Characteristic	**All (n=5590)**	**Underweight (n=219)**	**Healthy (n=3609)**	**Overweight (n=845)**	**Obese (n=922)**	**p-value**
Total	100%	3.8%	66.2%	15.3%	14.7%	
Gender, n (%)						0.5132
Male	2842 (51.1)	110 (48.3)	1823 (50.6)	422 (51.1)	487 (54.0)	
Female	2748 (48.9)	104 (51.7)	1786 (49.4)	423 (48.9)	435 (46.0)	
Race/Ethnicity[c], n (%)						<.0001
White	1552 (53.2)	56 (53.0)	1096 (56.6)	215 (51.6)	185 (39.7)	
Black	1376 (13.8)	53 (12.6)	877 (13.2)	195 (12.6)	251 (18.3)	
Hispanic	1949 (24.0)	58 (19.5)	1130 (20.9)	352 (28.7)	409 (34.3)	
Age, n (%)						<0.0001
2–5 years	2270 (39.3)	100 (34.5)	1593 (42.6)	310 (38.0)	267 (27.2)	
6–11 years	3320 (60.7)	114 (65.5)	2016 (57.4)	535 (62.0)	655 (72.8)	
Income[d], n (%)						0.0011
1st tertile	2491 (35.58)	80 (26.06)	1586 (34.32)	377 (36.79)	448 (42.42)	
2nd tertile	1587 (33.0)	63 (34.4)	1000 (32.7)	251 (33.6)	273 (33.2)	
3rd tertile	1134 (31.4)	55 (39.5)	795 (32.9)	155 (29.6)	129 (24.4)	
LCS Consumer, n (%)	1785 (34.6)	59 (26.7)	1108 (34.2)	274 (34.9)	344 (37.8)	0.0684
LCS Beverage Use, n (%)	1451 (28.3)	45 (20.1)	895 (27.9)	223 (28.2)	288 (32.3)	0.0558
LCS Food User, n (%)	484 (10.0)	18 (7.6)[g]	309 (10.2)	76 (10.1)	81 (9.3)	0.7168
Physical activity[e] (days per week)	6.1 ± 0.0	6.1 ± 0.2	6.3 ± 0.0	6.1 ± 0.1	5.7 ± 0.1	<0.001
Energy intake (kcal)	1756.3 ± 9.4	1674.6 ± 40.7	1743.5 ± 10.9	1753.5 ± 25.7	1837.5 ± 28.3	0.005
ADOLESCENTS (12–19 YEARS)						
Characteristic	**All (n=3671)**	**Underweight (n=115)**	**Healthy (n=2193)**	**Overweight (n=611)**	**Obese (n=752)**	**p-value**
Total	100%	3.1%	61.7%	15.6%	19.7%	
Gender, n (%)						0.1462
Male	1889 (51.1)	66 (65.3)	1131 (50.1)	306 (52.1)	386 (51.3)	

CHILDREN (2–11 YEARS)						
Characteristic	**All (n=5590)**	**Underweight (n=219)**	**Healthy (n=3609)**	**Overweight (n=845)**	**Obese (n=922)**	**p-value**
Female	1782 (48.9)	49 (34.7)	1062 (49.9)	305 (47.9)	366 (48.7)	
Race/Ethnicity, n (%)						0.0054
White	1008 (56.4)	34 (59.0)	644 (59.3)	141 (50.1)	189 (52.2)	
Black	927 (14.4)	23 (10.8)	526 (13.2)	164 (16.4)	214 (16.8)	
Hispanic	1240 (20.9)	35 (20.2)	696 (19.0)	233 (24.8)	276 (23.7)	
Income[b], n (%)						0.0001
1st tertile	1421 (30.3)	43 (28.8)	804 (27.6)	242 (33.6)	332 (36.4)	
2nd tertile	1113 (33.8)	39 (30.0)	646 (32.1)	188 (35.5)	240 (38.2)	
3rd tertile	836 (35.9)	27 (41.3)[g]	566 (40.2)	129 (30.9)	114 (25.4)	
LCS Consumer, n (%)	872 (28.2)	23 (21.0)[g]	496 (26.9)	149 (26.6)	204 (34.5)	0.0125
LCS Beverage Use, n (%)	744 (24.2)	20 (19.7)[g]	412 (22.2)	131 (24.5)	181 (31.1)	0.0065
LCS Food Use, n (%)	187 (5.4)	4 (2.0)[g]	114 (5.9)	26 (3.8)	43 (5.9)	0.1981
Physical activity[f] (MET-min per week)	2229.8 ± 58.1	1705.3 ± 337.6	2342.4 ± 77.6	2405.8 ± 176.3	1819.1 ± 136.3	0.009
Energy intake (kcal)	2046.1 ± 20.7	2239.2 ± 103.8	2097.9 ± 27.1	1992.4 ± 36.6	1895.6 ± 41.5	<0.001

[a] N reflects the number of participants in the sample, while percentages are weighted to account for the complex NHANES survey design.

[b] Defined based on standard body mass index (BMI, kg/m^2) cut-offs[12,13]

[c] Respondents reporting ‘other’ race (n=713 children, n=496 adolescents), including multi-racial, are included in overall estimates but are not shown separately.

[d] Defined based on tertiles of poverty-to-income ratio (PIR). N=378 children and N=301 adolescents were missing data for income.

[e] In children 2–11 years, physical activity was assessed as number of days physically active at least 60 min per week. N=11 children were missing data for physical activity.

[f] In adolescents 12–19 years, physical activity was assessed as MET-min of moderate and vigorous activity per week, which was derived using NHANES recommended MET score. N=110 adolescents were missing data for physical activity.

[g] Due to small sample size (n<30), these estimates may be unreliable and should be interpreted with caution.

Table 2

Characteristics of Child and Adolescent NHANES 2009–2014 Participants[a] by LCS Consumption

	Children 2–11 years			Adolescents 12–19 years		
	Consumers	**Non-consumers**	**p-value**	**Consumers**	**Non-consumers**	**p-value**
Gender, n (%)			0.0157			0.0031
Male	876 (48.7)	1966 (52.4)		435 (46.2)	1454 (53.1)	
Female	909 (51.3)	1839 (47.6)		437 (53.8)	1345 (46.9)	
Race/Ethnicity[b], n (%)			0.0011			<0.0001
White	550 (58.3)	1002 (50.6)		312 (66.6)	696 (52.5)	
Black	409 (12.2)	967 (14.7)		198 (10.7)	729 (15.8)	
Hispanic	623 (22.1)	1326 (25.0)		269 (16.6)	971 (22.5)	
Age, n (%)			<0.001			N/A
2–5y	627 (33.5)	1643 (42.4)		N/A[d]	N/A	
6–11y	1158 (66.5)	2162 (57.6)		N/A	N/A	
Income, n (%)[c]			0.0066			0.0009
1st tertile	730 (31.4)	1761 (37.8)		302 (24.3)	1119 (32.7)	
2nd tertile	524 (33.6)	1063 (32.7)		276 (34.4)	837 (33.5)	
3rd tertile	431 (34.9)	703 (29.5)		234 (41.3)	602 (33.8)	
Weight status[d], n (%)			0.0684			0.0125
Underweight	59 (2.9)	155 (4.2)		23 (2.3)[h]	92 (3.4)	
Healthy	1108 (65.5)	2501 (66.5)		496 (58.9)	1697 (62.8)	
Overweight	274 (15.5)	571 (15.2)		149 (14.7)	462 (15.9)	
Obese	344 (16.1)	578 (14.0)		204 (24.1)	548 (17.9)	
Physical activity[f,g]	6.1 (0.1)	6.2 (0.1)	0.6318	2192 (88.7)	2244 (66.7)	0.6064
Energy intake (kcal)	1789 (15.5)	1739 (9.9)	0.0046	2032 (33.3)	2051 (24.8)	0.6338

[a]N reflects the number of participants in the sample, while percentages are weighted to account for the complex NHANES survey design.

[b]Respondents reporting ‘other’ race (n=713 children, n=496 adolescents), including multi-racial, are included in overall estimates but are not shown separately.

[c]Defined based on tertiles of poverty-to-income ratio (PIR)

[d]Defined based on standard body mass index (BMI, kg/m^2) cut-offs[12,13]

[e]N/A indicates that age sub-group comparisons were not performed for adolescents

[f]In children 2–11 years, physical activity was assessed as number of days physically active at least 60 min per week.

[g]In adolescents 12–19 years, physical activity was assessed as MET-min of moderate and vigorous activity per week, which was derived using NHANES recommended MET score.

[h]Due to small sample size ($n<30$), these estimates may be unreliable and should be interpreted with caution.

Table 3

Unadjusted and Adjusted Odds of Obesity by LCS Consumption among NHANES 2009–2014 Participants

	Any LCS		LCS Beverages		LCS Foods	
	OR (95% CI)		OR (95% CI)		OR (95% CI)	
	Unadjusted	Adjusted[1]	Unadjusted	Adjusted[1]	Unadjusted	Adjusted[1]
Children (2–11 years)						
All (n=5, 590)	1.18 (0.97, 1.44)	1.19 (0.97, 1.46)	**1.25 (1.01, 1.56)**	1.24 (0.98, 1.56)	0.91 (0.68, 1.23)	0.99 (0.73, 1.34)
Sex						
Male (n=2, 842)	1.21 (0.93,1.59)	1.24 (0.94, 1.63)	**1.42 (1.08, 1.88)**	**1.45 (1.09, 1.93)**	0.79 (0.50, 1.23)	0.87 (0.55, 1.37)
Female (n=2, 748)	1.16 (0.89, 1.51)	1.13 (0.84, 1.52)	1.09 (0.81, 1.47)	1.02 (0.74, 1.42)	1.06 (0.70, 1.63)	1.13 (0.75, 1.72)
Age Group						
2–5 years (n=2270)	1.33 (0.96, 1.87)	1.28 (0.92, 1.79)	1.48 (1.00, 2.18)	1.35 (0.89, 2.05)	0.84 (0.47, 1.52)	0.87 (0.47, 1.61)
6–11 years (n=3320)	1.05 (0.85, 1.28)	1.13 (0.91, 1.41)	1.09 (0.87, 1.37)	1.17 (0.91, 1.50)	0.94 (0.65, 1.37)	1.03 (0.72, 1.49)
Race/Ethnicity						
White (n=1,552)	1.04 (0.72, 1.50)	0.99 (0.68, 1.44)	1.16 (0.77, 1.76)	1.09 (0.71, 1.67)	0.93 (0.56, 1.53)	0.93 (0.57, 1.52)
Black (n=1,376)	1.25 (0.84, 1.87)	1.21 (0.82, 1.80)	1.11 (0.73, 1.71)	1.06 (0.69, 1.61)	1.35 (0.81, 2.25)	1.46 (0.86, 2.49)
Hispanic (n=1,949)	**1.57 (1.19, 2.08)**	**1.59 (1.20, 2.10)**	**1.68 (1.26, 2.26)**	**1.66 (1.23, 2.24)**	0.87 (0.58, 1.31)	0.86 (0.60, 1.25)
Income						
1st tertile (n=2,491)	1.23 (0.91, 1.65)	1.23 (0.92, 1.64)	1.18 (0.89, 1.56)	1.16 (0.88, 1.53)	1.13 (0.64, 1.99)	1.19 (0.68, 2.11)
2nd tertile (n= 1,587)	1.27(0.79, 2.04)	1.28 (0.78, 2.07)	1.43 (0.90, 2.28)	1.44 (0.88, 2.36)	0.84 (0.47, 1.52)	0.89 (0.50, 1.60)
3rd tertile (n= 1,134)	1.11 (0.67, 1.82)	1.06 (0.62, 1.82)	1.23 (0.76, 1.99)	1.14 (0.67, 1.92)	0.89 (0.46, 1.74)	0.94 (0.48, 1.84)
Adolescents (12–19 years)						
All (n= 3, 671)	**1.45 (1.15, 1.83)**	**1.57 (1.23, 2.01)**	**1.55 (1.17, 2.06)**	**1.71 (1.31, 2.23)**	1.12 (0.64, 1.97)	1.10 (0.61, 1.96)
Sex						
Male (n= 1,889)	**1.86 (1.32, 2.64)**	**1.92 (1.35, 2.72)**	**1.94 (1.28, 2.95)**	**2.03 (1.33, 3.08)**	1.74 (0.98, 3.09)	1.66 (0.90, 3.05)
Female (n= 1,782)	1.14 (0.88, 1.49)	**1.32 (1.01, 1.73)**	1.25 (0.95, 1.66)	**1.46 (1.13, 1.89)**	0.73 (0.34, 1.57)	0.73 (0.31, 1.71)
Race/Ethnicity[2]						
White (n= 1,008)	**1.81 (1.26, 2.60)**	**1.95 (1.35, 2.82)**	**1.99 (1.33, 2.99)**	**2.17 (1.50, 3.15)**	1.14 (0.50, 2.60)	1.12 (0.47, 2.67)
Black (n= 927)	0.99 (0.68, 1.43)	1.01 (0.68, 1.49)	1.06 (0.70, 1.62)	1.17 (0.78, 1.75)	0.81 (0.42, 1.58)	0.69 (0.37, 1.28)

	Any LCS		LCS Beverages		LCS Foods	
	OR (95% CI)		OR (95% CI)		OR (95% CI)	
	Unadjusted	**Adjusted**[1]	**Unadjusted**	**Adjusted**[1]	**Unadjusted**	**Adjusted**[1]
Hispanic (n= 1,240)	1.27 (0.85, 1.89)	1.34 (0.88, 2.06)	1.17 (0.80, 1.72)	1.23 (0.82, 1.85)	1.53 (0.65, 3.60)	1.69 (0.69, 4.10)
Income						
1st tertile (n= 1,421)	**1.48 (1.03, 2.12)**	1.39 (0.97, 2.01)	**1.46 (1.05, 2.04)**	1.35 (0.96, 1.89)	1.42 (0.59, 3.41)	1.35 (0.61, 3.00)
2nd tertile (n= 1,113)	1.61 (0.96, 2.70)	**1.77 (1.08, 2.91)**	**1.83 (1.04, 3.24)**	**1.99 (1.13, 3.49)**	0.93 (0.44, 1.98)	0.99 (0.47, 2.06)
3rd tertile (n= 836)	1.46 (0.86, 2.47)	1.71 (0.99, 2.93)	**1.69 (1.00, 2.87)**	**1.95 (1.14, 3.33)**	0.96 (0.31, 2.96)	1.13 (0.36, 3.50)

[1] Adjusted model included the following covariates: age, sex, race/ethnicity, income, total energy intake, and physical activity.

[2] Respondents reporting ‘other’ race (n=713 children, n=496 adolescents), including multi-racial, are included in overall estimates but are not shown separately.

Values in bold are statistically significant

[*] Values were rounded to the nearest hundredth and thus, the lower bound of the 95% confidence interval was below 1.00 prior to rounding.