

detect a difference in the time health care providers took to answer questions from APSO vs SOAP notes. Further studies are needed to determine whether these outpatient findings at one center can apply to another, or to inpatient or emergency department settings, or even to radiology and pathology reports. Readability of EHR notes will be increasingly important as more organizations adopt EHRs. This study demonstrates that a structural change in the health care provider EHR progress note, from SOAP to APSO format, is feasible and generally well received.

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## Hypertriglyceridemia and Acute Pancreatitis

**A**cute pancreatitis (AP) is common and potentially serious.<sup>1</sup> Common causes are gallstones and alcohol abuse; other causes include medications, common bile duct obstruction, trauma, and hypertriglyceridemia.<sup>2</sup> Although the association between hypertriglyceridemia and AP is well established, estimates of risk are based on case series and studies of high-risk groups.<sup>3-5</sup> The risk of AP from hypertriglyceridemia in the general population is not well characterized. We report results from a cohort study using record-linkage methods to estimate the risk and relative burden of AP in patients with differing degrees of hypertriglyceridemia.

**Methods.** We used databases in the Medicines Monitoring Unit of our institution that included dispensed community prescriptions, hospital discharge data, regional laboratory data, and other data. The study population consisted of residents of Tayside, Scotland, who were registered with a primary care physician between 1993 and 2007 and remained resident in Tayside or died during the study period. Study subjects had at least 1 serum triglyceride measurement between 1993 and 2007, entered the study on the date of their highest triglyceride measurement during the study period, and were categorized by triglyceride concentration into 1 of the following 3 cohorts: 149 mg/dL or lower (group 1); 150 to 499 mg/dL (group 2); or 500 mg/dL or higher (group 3). (To convert triglycerides to millimoles per liter, multiply by 0.0113.)

The primary study outcome was incident AP during follow-up (hospitalization with a primary diagnosis of AP or serum amylase activity of 300 U/L or higher during follow-up [reference interval, 0-100 U/L]). Data were summarized as mean (SD), or number of subjects (percentage).

A Cox regression model was constructed to adjust for potential confounders; data were expressed as hazard ratios (HRs) with 95% CIs. Covariates were age at study entry; sex; socioeconomic status; concentrations of total and high-density lipoprotein (HDL) cholesterol; comorbidities of gallstones, other biliary disease, diabetes, alcohol-related liver disease, alcoholic cirrhosis, alcoholic hepatitis,<sup>6</sup> alcohol hospitalization, chronic pancreatitis, and renal failure; and use during follow-up of gastrointestinal drugs, diuretics, lipid-regulating drugs, analgesics, sodium valproate, antibacterial drugs, corticosteroids, estrogens and hormone therapy, and musculoskeletal and joint disease drugs. The Scottish Index of Multiple Deprivation<sup>7</sup> was used as a measure of socioeconomic status. Population-attributable risks (PARs) were calculated for each triglyceride group and other AP risk factors. Sensitivity analyses were performed by (1) excluding subjects with hospitalization for gallstones, chronic pancreatitis, renal failure, alcohol morbidities, other biliary disease, and not adjusting for concentrations of

**Table. Univariate and Multivariate Hazard Ratios for First AP Admission**

Characteristics	Hazard Ratio (95% CI)	
	Univariate	Multivariate
Age, y	1.02 (1.01-1.03) <sup>a</sup>	1.03 (1.02-1.04) <sup>b</sup>
Sex (male vs female)	1.09 (0.88-1.36)	1.00 (0.77-1.28)
TG concentration group <sup>c</sup>		
1 (≤150 mg/dL)	1 [Reference]	1 [Reference]
2 (150-499 mg/dL)	1.39 (1.10-1.76) <sup>b</sup>	1.50 (1.14-1.97) <sup>b</sup>
3 (≥500 mg/dL)	2.72 (1.88-3.95) <sup>a</sup>	3.20 (1.99-5.16) <sup>a</sup>
TG concentration (per 100 mg/dL)	1.05 (1.04-1.06) <sup>a</sup>	1.04 (1.02-1.05) <sup>a</sup>
TC concentration (per 100 mg/dL)	1.07 (0.87-1.32)	0.93 (0.75-1.15)
HDL concentration (per 100 mg/dL)	0.76 (0.38-1.49)	1.52 (0.69-3.32)
Socioeconomic status		
1 (Most deprived)	1 [Reference]	1 [Reference]
2-3	1.02 (0.77-1.37)	0.98 (0.72-1.32)
4-5 (Most affluent)	0.78 (0.58-1.05)	0.80 (0.59-1.10)
Concurrent use of drugs		
Analgesics	1.01 (0.81-1.25)	1.15 (0.88-1.50)
Antibacterial drugs	0.44 (0.35-0.55) <sup>a</sup>	0.43 (0.33-0.55) <sup>a</sup>
Tetracyclines	0.44 (0.28-0.70) <sup>a</sup>	0.53 (0.33-0.86) <sup>a</sup>
Sulfonamides and trimethoprim	0.65 (0.48-0.87) <sup>a</sup>	0.60 (0.43-0.82) <sup>a</sup>
Diuretics	0.89 (0.71-1.11)	0.74 (0.57-0.95) <sup>b</sup>
Thiazides and related diuretics	0.61 (0.46-0.80) <sup>a</sup>	0.57 (0.43-0.75) <sup>a</sup>
Loop diuretics	1.15 (0.88-1.51)	0.88 (0.65-1.20)
Gastrointestinal tract drugs	1.26 (0.94-1.70)	1.33 (0.96-1.85)
Dyspepsia and gastroesophageal reflux disease	1.75 (1.07-2.88) <sup>b</sup>	1.34 (0.75-2.35)
Antispasmodics and other drugs altering gut motility	0.89 (0.33-2.40)	0.72 (0.26-2.01)
Antisecretory drugs and mucosal protectants	1.41 (1.03-1.93) <sup>b</sup>	1.44 (0.99-2.08)
Acute diarrhea	0.50 (0.07-3.53)	0.37 (0.05-2.75)
Chronic bowel disorders	1.63 (0.41-6.56)	2.32 (0.55-9.78)
Laxatives	1.47 (0.88-2.45)	1.19 (0.68-2.07)
Local preparations for anal and rectal disorders	2.07 (0.85-5.03)	2.52 (1.00-6.31)
Drugs affecting intestinal secretions	3.56 (0.50-25.41)	0.77 (0.09-6.46)

(continued)

total and HDL cholesterol; (2) using the date of first, or lowest, measured triglyceride concentration as the entry date; and (3) using average triglyceride concentration during follow-up for categorization.

**Results.** There were 31 740 subjects in group 1, 31 887 in group 2, 3642 in group 3. There were 116 AP events in group 1, 178 in group 2, and 37 in group 3 during the 127 473, 143 495, and 14 935 person-years of follow-up, respectively. Crude incidence of AP was 0.91 per 1000 person-years (95% CI, 0.76-1.09) in group 1, 1.24 (95% CI, 1.07-1.44) in group 2, and 2.48 (95% CI, 1.79-3.42) in group 3. The proportion of incident AP cases exposed to moderate hypertriglyceridemia (150-499 mg/dL) was 0.54; for severe hypertriglyceridemia (≥500 mg/

**Table. Univariate and Multivariate Hazard Ratios for First AP Admission (continued)**

Characteristics	Hazard Ratio (95% CI)	
	Univariate	Multivariate
Concurrent use of drugs (continued)		
Lipid-regulating drugs		
Untreated groups	1 [Reference]	1 [Reference]
Statins	0.70 (0.56-0.87) <sup>a</sup>	0.53 (0.41-0.69) <sup>a</sup>
Other lipid-lowering drugs	2.55 (1.39-4.69) <sup>a</sup>	1.88 (0.99-3.53)
Both statins and other lipid-lowering drugs	1.75 (0.82-3.75)	0.92 (0.41-2.06)
Musculoskeletal and joint drugs		
Nonsteroidal anti-inflammatory drugs	0.59 (0.47-0.73) <sup>a</sup>	0.55 (0.43-0.70) <sup>a</sup>
Drugs that suppress rheumatic disease process	0.66 (0.21-2.06)	0.82 (0.26-2.64)
Drugs used in neuromuscular disorders	1.23 (0.51-2.98)	1.49 (0.60-3.72)
Drugs for relief of soft-tissue inflammation	0.78 (0.56-1.07)	0.65 (0.46-0.92) <sup>b</sup>
Estrogens and hormone replacement	0.72 (0.46-1.12)	0.83 (0.51-1.35)
Sodium valproate	1.28 (0.53-3.11)	0.99 (0.39-2.52)
Corticosteroids	0.78 (0.61-0.99) <sup>a</sup>	0.95 (0.73-1.23)
Comorbidity		
Alcohol hospitalization	5.65 (3.18-10.06) <sup>a</sup>	4.81 (2.56-9.06) <sup>a</sup>
Gallstones	7.19 (5.28-9.79) <sup>a</sup>	6.48 (4.62-9.09) <sup>a</sup>
Other biliary disease	5.65 (3.31-9.64) <sup>a</sup>	2.32 (1.31-4.10) <sup>a</sup>
Renal failure	3.83 (2.35-6.25) <sup>a</sup>	3.78 (2.28-6.25) <sup>a</sup>
Chronic pancreatitis	70.11 (41.76-117.71) <sup>a</sup>	28.91 (14.85-55.29) <sup>a</sup>
Diabetes	1.33 (1.01-1.77) <sup>b</sup>	1.21 (0.89-1.65)

Abbreviations: AP, acute pancreatitis; HDL, high-density lipoprotein cholesterol level; TC, total cholesterol level; TG, triglyceride level. SI conversion factors: To convert TG to millimoles per liter, multiply by 0.0113; TC and HDL to millimoles per liter, multiply by 0.0259.

<sup>a</sup>  $P < .01$ .

<sup>b</sup>  $P < .05$ .

<sup>c</sup>  $P < .001$  for trend among the 3 groups.

dL), it was 0.11. Corresponding PARs were 18.37% and 7.74%.

The **Table** lists results of univariate and multivariate Cox regression analysis for incident AP admission. There was a significant dose-response relationship between triglyceride concentration and incident AP (adjusted HR, 1.04 [95% CI, 1.02-1.05]). Compared with group 1, the adjusted HR for AP was 1.50 (95% CI, 1.14-1.97) for group 2 and 3.20 (95% CI, 1.99-5.16) for group 3. People who were older, had gallstones, renal failure, chronic pancreatitis, or other biliary disease had a higher risk of incident AP. Use of statins, antibacterial drugs, diuretics, or musculoskeletal joint drugs was associated with a lower risk. The risk of incident AP increased by 4% for every 100-mg/dL increase in triglyceride concentration (after

adjustment for covariates and removal of patients hospitalized for gallstones, chronic pancreatitis, alcohol-related morbidities, renal failure, and other biliary disease). The HR for AP associated with severe hypertriglyceridemia ( $\geq 500$  mg/dL) was higher than the HR associated with moderate hypertriglyceridemia (150-499 mg/dL). A much greater proportion of AP cases was exposed to moderate rather than severe hypertriglyceridemia, explaining why the PAR of AP attributable to moderate hypertriglyceridemia was 18.37% compared with 7.74%.

**Comment.** This study was population-based, with long follow-up (15 years) and low migration. We validated the 82% of cases where records were retrievable and confirmed the accuracy of diagnosis in 95.3%. We adjusted for an extensive range of confounders and performed a wide range of sensitivity analyses to test the robustness of the relationship between triglyceride concentration and incident AP. However, unmeasured confounders may have influenced the results. Nevertheless, observational studies are the only realistic approach to study this association given the low incidence of AP (about 1 per 1000 person-years of follow-up). Our findings that statins were associated with reduced risk of incident AP are consistent with the results of a recent meta-analysis of 28 randomized controlled trials of lipid-modifying drugs.<sup>8</sup>

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## Availability of DMAA Supplements Despite US Food and Drug Administration Action

The stimulant DMAA, also known as 1,3-dimethylamylamine, has been the subject of much controversy.<sup>1</sup> In the United States, it is currently marketed as a dietary supplement, primarily in products promoted as a preworkout supplement for boosting strength, energy, and power. Two of the most prominent supplements containing DMAA are “Jack3d” and “OxyELITE Pro” (USP Labs) However, there are over 250 commercial dietary supplements containing DMAA on the market.<sup>2</sup>

As has been reported elsewhere,<sup>1</sup> DMAA supplements are immensely popular among consumers. However, there is great concern among health professionals and regulators for several reasons. First, it is unlikely that DMAA is truly of natural origin. Therefore, its marketing as a dietary supplement may be illegitimate. Second, there are significant safety concerns. To date, there have been over 40 reports of serious adverse events, including at least 2 reports of death.<sup>2,3</sup>

On April 27, 2012, the US Food and Drug Administration (FDA) sent warning letters to 10 manufacturers of 16 products containing DMAA. The warning indicated that the products were considered adulterated because DMAA is considered a new dietary ingredient (NDI).<sup>3</sup> NDIs require the manufacturer to submit some documentation demonstrating the expectation of safety. Without such documentation, the FDA considered the products to be adulterated, unapproved drugs.

It came to my attention on May 17, 2012, that some of these products were still available for sale through on-

**Table. DMAA-Containing Product Availability**

Product	Manufacturer	Availability	
		From Manufacturer	From Retailer
Biorhythm SSIN Juice	Exclusive Supplements	No	Yes
Code Red	MuscleMeds	No	Yes
Hemo Rage Black	Nutrex Research	No	Yes
Jack3d	USP Labs	Yes	Yes
Lean Efx	Fahrenheit Nutrition	Yes	Yes
Lipo-6 Black Ultra	Nutrex Research	No	Yes
Lipo-6 Black	Nutrex Research	No	Yes
Lipo-6 Black Hers Ultra	Nutrex Research	No	Yes
Lipo-6 Black Hers	Nutrex Research	No	Yes
MethylHex 4,2	SEI Pharmaceuticals	Yes	Yes
Napalm	Muscle Warfare	Yes	Yes
Nitric Blast	SNI LLC	No	Yes
OxyELITE Pro	USP Labs	Yes	Yes
PWR	iSatori	Yes	Yes
SpiroDEX	Gaspari Nutrition	No	Yes

Abbreviation: DMAA, 1,3-dimethylamylamine.