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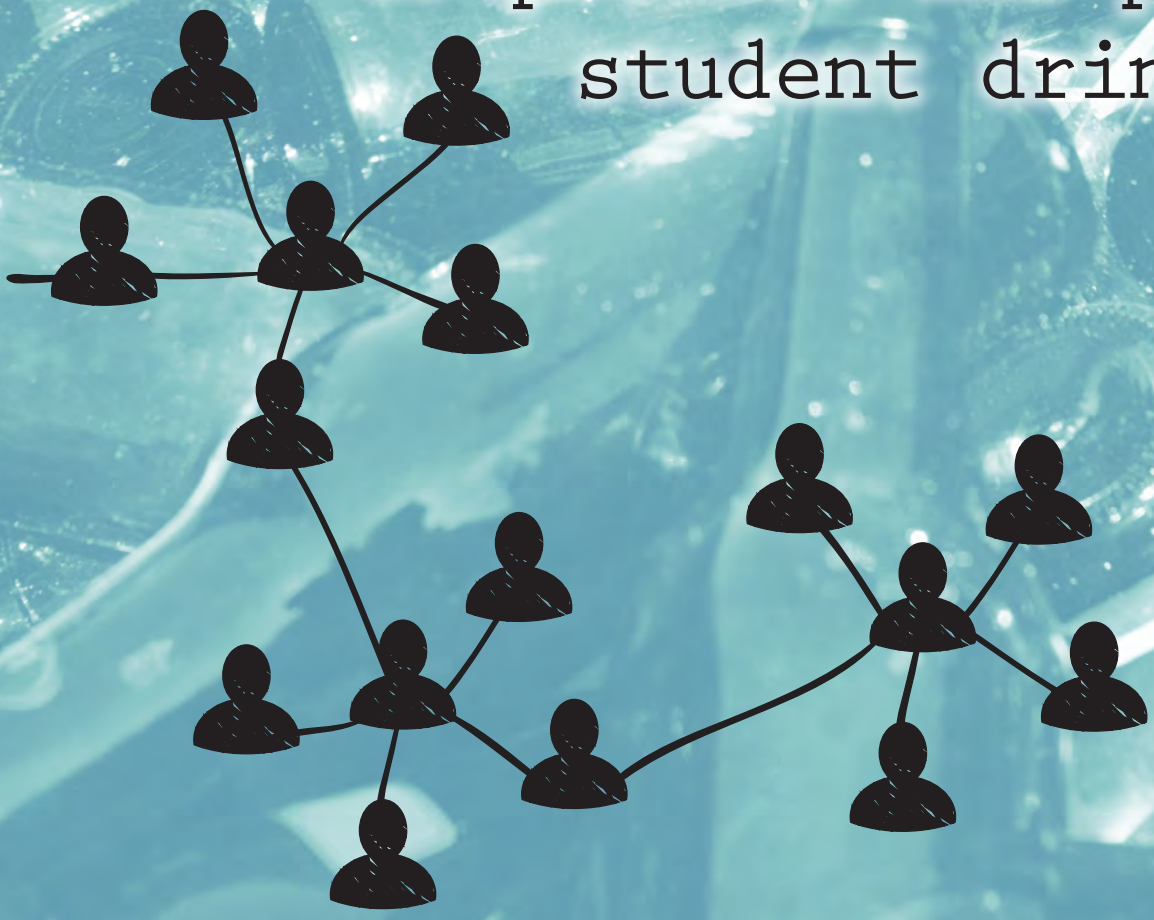
WMJ

volume 112 · no. 6 · december 2013

# Social media and alcohol

## Exploring strategies to predict and prevent student drinking

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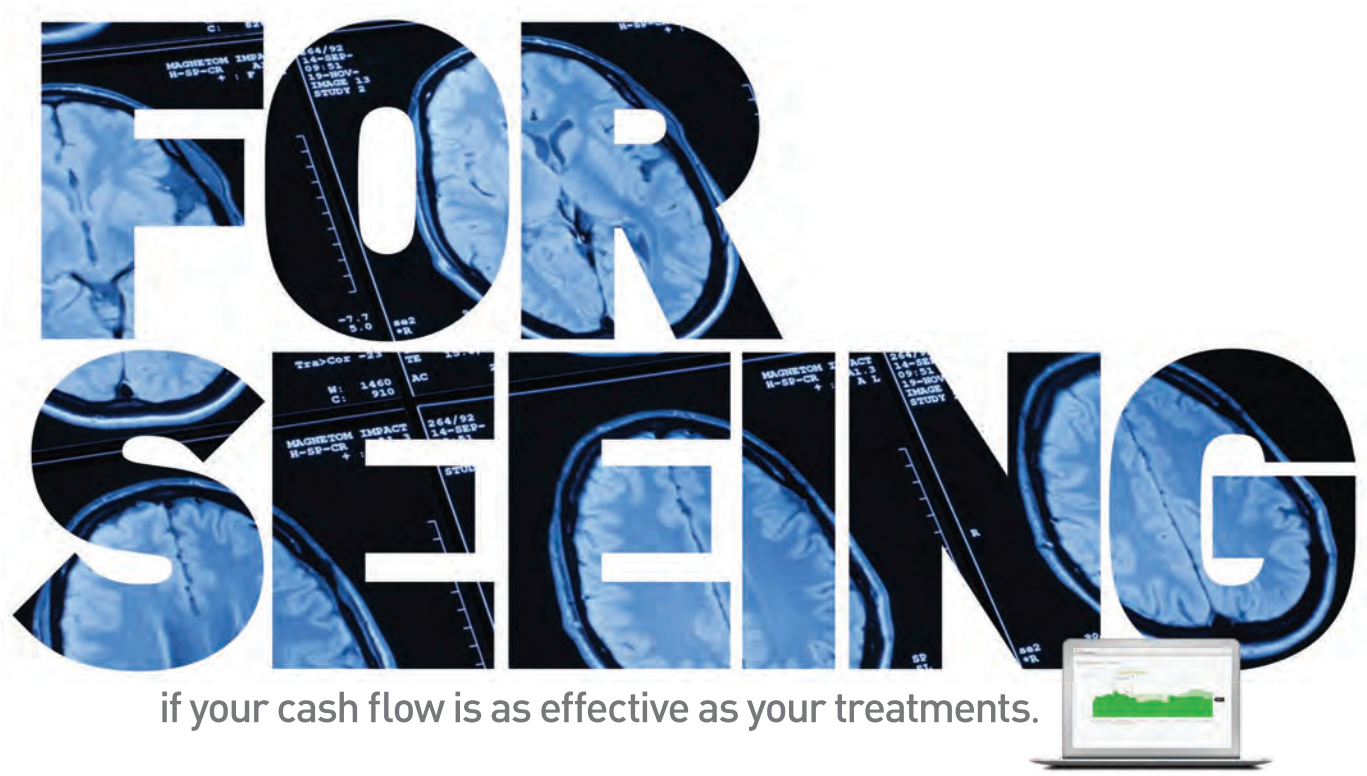


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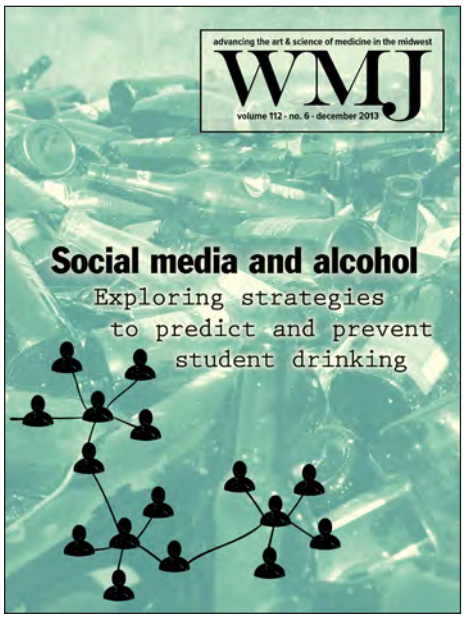
# WMJ




## COVER THEME
## Social media and alcohol: Exploring strategies to predict and prevent student drinking

It's reported that up to 98% of college students use Facebook, and references to alcohol use are common on this and other social media sites. In this issue of *WMJ,* researchers explore associations between such social media displays and alcohol use by students and consider strategies for using this medium for targeted prevention messages.

**Cover design by Mary Kay Adams-Edgette.**



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# advancing the art & science of medicine in the midwest

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# In Memoriam: J.F.K.

D.N. Goldstein, MD, Editorial Director

*Editor's note: The following is an editorial published in* WMJ, *Volume 62, p. 515, December 1963.*

The few weeks that have elapsed since the assassination of President John F. Kennedy have done nothing to dim the horror of that tragic Friday noon. When the chilling news flashed through the country, most Americans asked themselves the most unanswerable of all questions: why? Why—in the most civilized country in the world, with the longest history of democratic process—is the head of state removed by violence? Why—in the Ultimate Plan—is a young, deranged punk with a mail-order rifle permitted to snuff out the life of the man that the majority of people in this country had elected as their leader? Why?

All that sad weekend millions of Americans listened to radio reports and watched the same news films on television, even though it was known the terrible fact would be unchanged the fourth, fifth, or sixth time the same story unfolded. It was as though some hint could be found to the Why question in the numberless retelling of the story. But the hint never came, and the answer will always elude us.

But now that the deed is done and the body of John F. Kennedy is at rest, perhaps we can take a moral step forward as a result of the assassination. We can determine to hate hate as much as the haters hated him and the socially oriented program he stood for. We can strive to eliminate the curse of extremism from our midst which created the poisonous atmosphere that nourished that deranged mind in Dallas.

We do honor the memory of John F. Kennedy by extirpating in ourselves, as a starter, those unreasonable impulses of enmity that grow to frenzied passions. We can calm the extreme statement that creates the rationale for acts of violence. In memory of J.F.K., we can resubscribe to the moral system he represented.

"Teach us, O Lord, to hate evil."

—D.N.G.

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†**Victoza® is not indicated for the management of obesity, and weight change was a secondary end point in clinical trials.**

VICTOZA®
liraglutide (rDNA origin) injection

## Indications and Usage

Victoza® (liraglutide [rDNA origin] injection) is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.

Because of the uncertain relevance of the rodent thyroid C-cell tumor findings to humans, prescribe Victoza® only to patients for whom the potential benefits are considered to outweigh the potential risk. Victoza® is not recommended as first-line therapy for patients who have inadequate glycemic control on diet and exercise.

Based on spontaneous postmarketing reports, acute pancreatitis, including fatal and non-fatal hemorrhagic or necrotizing pancreatitis has been observed in patients treated with Victoza®. Victoza® has not been studied in patients with a history of pancreatitis. It is unknown whether patients with a history of pancreatitis are at increased risk for pancreatitis while using Victoza®. Other antidiabetic therapies should be considered in patients with a history of pancreatitis.

Victoza® is not a substitute for insulin. Victoza® should not be used in patients with type 1 diabetes mellitus or for the treatment of diabetic ketoacidosis, as it would not be effective in these settings.

Victoza® has not been studied in combination with prandial insulin.

## Important Safety Information

**Liraglutide causes dose-dependent and treatment-duration-dependent thyroid C-cell tumors at clinically relevant exposures in both genders of rats and mice. It is unknown whether Victoza® causes thyroid C-cell tumors, including medullary thyroid carcinoma (MTC), in humans, as human relevance could not be ruled out by clinical or nonclinical studies. Victoza® is contraindicated in patients with a personal or family history of MTC and in patients with Multiple Endocrine Neoplasia syndrome type 2 (MEN 2). Based on the findings in rodents, monitoring with serum calcitonin or thyroid ultrasound was performed during clinical trials, but this may have increased the number of unnecessary thyroid surgeries. It is unknown whether monitoring with serum calcitonin or thyroid ultrasound will mitigate human risk of thyroid C-cell tumors. Patients should be counseled regarding the risk and symptoms of thyroid tumors.**

Do not use in patients with a prior serious hypersensitivity reaction to Victoza® (liraglutide [rDNA origin] injection) or to any of the product components.

Postmarketing reports, including fatal and non-fatal hemorrhagic or necrotizing pancreatitis. Discontinue promptly if pancreatitis is suspected. Do not restart if pancreatitis is confirmed. Consider other antidiabetic therapies in patients with a history of pancreatitis.

When Victoza® is used with an insulin secretagogue (e.g. a sulfonylurea) or insulin serious hypoglycemia can occur. Consider lowering the dose of the insulin secretagogue or insulin to reduce the risk of hypoglycemia.

Renal impairment has been reported postmarketing, usually in association with nausea, vomiting, diarrhea, or dehydration which may sometimes require hemodialysis. Use caution when initiating or escalating doses of Victoza® in patients with renal impairment.

Serious hypersensitivity reactions (e.g. anaphylaxis and angioedema) have been reported during postmarketing use of Victoza®. If symptoms of hypersensitivity reactions occur, patients must stop taking Victoza® and seek medical advice promptly.

There have been no studies establishing conclusive evidence of macrovascular risk reduction with Victoza® or any other antidiabetic drug.

The most common adverse reactions, reported in ≥5% of patients treated with Victoza® and more commonly than in patients treated with placebo, are headache, nausea, diarrhea, dyspepsia, constipation and anti-liraglutide antibody formation. Immunogenicity-related events, including urticaria, were more common among Victoza®-treated patients (0.8%) than among comparator-treated patients (0.4%) in clinical trials.

Victoza® has not been studied in type 2 diabetes patients below 18 years of age and is not recommended for use in pediatric patients.

There is limited data in patients with renal or hepatic impairment.

**Please see brief summary of Prescribing Information on adjacent page.**


0513-00015590-1 June 2013

**Victoza® (liraglutide [rDNA origin] injection)**
**Rx Only**
**BRIEF SUMMARY. Please consult package insert for full prescribing information.**

**WARNING: RISK OF THYROID C-CELL TUMORS:** Liraglutide causes dose-dependent and treatment-duration-dependent thyroid C-cell tumors at clinically relevant exposures in both genders of rats and mice. It is unknown whether Victoza® causes thyroid C-cell tumors, including medullary thyroid carcinoma (MTC), in humans, as human relevance could not be ruled out by clinical or nonclinical studies. Victoza® is contraindicated in patients with a personal or family history of MTC and in patients with Multiple Endocrine Neoplasia syndrome type 2 (MEN 2). Based on the findings in rodents, monitoring with serum calcitonin or thyroid ultrasound was performed during clinical trials, but this may have increased the number of unnecessary thyroid surgeries. It is unknown whether monitoring with serum calcitonin or thyroid ultrasound will mitigate human risk of thyroid C-cell tumors. Patients should be counseled regarding the risk and symptoms of thyroid tumors *[see Contraindications and Warnings and Precautions].*

**INDICATIONS AND USAGE:** Victoza® is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus. **Important Limitations of Use:** Because of the uncertain relevance of the rodent thyroid C-cell tumor findings to humans, prescribe Victoza® only to patients for whom the potential benefits are considered to outweigh the potential risk. Victoza® is not recommended as first-line therapy for patients who have inadequate glycemic control on diet and exercise. Based on spontaneous postmarketing reports, acute pancreatitis, including fatal and non-fatal hemorrhagic or necrotizing pancreatitis has been observed in patients treated with Victoza®. Victoza® has not been studied in patients with a history of pancreatitis. It is unknown whether patients with a history of pancreatitis are at increased risk for pancreatitis while using Victoza®. Other antidiabetic therapies should be considered in patients with a history of pancreatitis. Victoza® is not a substitute for insulin. Victoza® should not be used in patients with type 1 diabetes mellitus or for the treatment of diabetic ketoacidosis, as it would not be effective in these settings. The concurrent use of Victoza® and prandial insulin has not been studied.

**CONTRAINDICATIONS:** Do not use in patients with a personal or family history of medullary thyroid carcinoma (MTC) or in patients with Multiple Endocrine Neoplasia syndrome type 2 (MEN 2). Do not use in patients with a prior serious hypersensitivity reaction to Victoza® or to any of the product components.

**WARNINGS AND PRECAUTIONS: Risk of Thyroid C-cell Tumors:** Liraglutide causes dose-dependent and treatment-duration-dependent thyroid C-cell tumors (adenomas and/or carcinomas) at clinically relevant exposures in both genders of rats and mice. Malignant thyroid C-cell carcinomas were detected in rats and mice. A statistically significant increase in cancer was observed in rats receiving liraglutide at 8-times clinical exposure compared to controls. It is unknown whether Victoza® will cause thyroid C-cell tumors, including medullary thyroid carcinoma (MTC), in humans, as the human relevance of liraglutide-induced rodent thyroid C-cell tumors could not be determined by clinical or nonclinical studies. In the clinical trials, there have been 6 reported cases of thyroid C-cell hyperplasia among Victoza®-treated patients and 2 cases in comparator-treated patients (1.3 vs. 1.0 cases per 1000 patient-years). One comparator-treated patient with MTC had pre-treatment serum calcitonin concentrations >1000 ng/L suggesting pre-existing disease. All of these cases were diagnosed after thyroidectomy, which was prompted by abnormal results on routine, protocol-specified measurements of serum calcitonin. Five of the six Victoza®-treated patients had elevated calcitonin concentrations at baseline and throughout the trial. One Victoza® and one non-Victoza®-treated patient developed elevated calcitonin concentrations while on treatment. Calcitonin, a biological marker of MTC, was measured throughout the clinical development program. The serum calcitonin assay used in the Victoza® clinical trials had a lower limit of quantification (LLOQ) of 0.7 ng/L and the upper limit of the reference range was 5.0 ng/L for women and 8.4 ng/L for men. At Weeks 26 and 52 in the clinical trials, adjusted mean serum calcitonin concentrations were higher in Victoza®-treated patients compared to placebo-treated patients but not compared to patients receiving active comparator. At these timepoints, the adjusted mean serum calcitonin values (~1.0 ng/L) were just above the LLOQ with between-group differences in adjusted mean serum calcitonin values of approximately 0.1 ng/L or less. Among patients with pre-treatment serum calcitonin below the upper limit of the reference range, shifts to above the upper limit of the reference range which persisted in subsequent measurements occurred most frequently among patients treated with Victoza® 1.8 mg/day. In trials with on-treatment serum calcitonin measurements out to 5-6 months, 1.9% of patients treated with Victoza® 1.8 mg/day developed new and persistent calcitonin elevations above the upper limit of the reference range compared to 0.8-1.1% of patients treated with control medication or the 0.6 and 1.2 mg doses of Victoza®. In trials with on-treatment serum calcitonin measurements out to 12 months, 1.3% of patients treated with Victoza® 1.8 mg/day had new and persistent elevations of calcitonin from below or within the reference range to above the upper limit of the reference range, compared to 0.6%, 0% and 1.0% of patients treated with Victoza® 1.2 mg, placebo and active control, respectively. Otherwise, Victoza® did not produce consistent dose-dependent or time-dependent increases in serum calcitonin. Patients with MTC usually have calcitonin values >50 ng/L. In Victoza® clinical trials, among patients with pre-treatment serum calcitonin <50 ng/L, one Victoza®-treated patient and no comparator-treated patients developed serum calcitonin >50 ng/L. The Victoza®-treated patient who developed serum calcitonin >50 ng/L had an elevated pre-treatment serum calcitonin of 10.7 ng/L that increased to 30.7 ng/L at Week 12 and 53.5 ng/L at the end of the 6-month trial. Follow-up serum calcitonin was 22.3 ng/L more than 2.5 years after the last dose of Victoza®. The largest increase in serum calcitonin in a comparator-treated patient was seen with glimepiride in a patient whose serum calcitonin increased from 19.3 ng/L at baseline to 44.8 ng/L at Week 65 and 38.1 ng/L at Week 104. Among patients who began with serum calcitonin <20 ng/L, calcitonin elevations to >20 ng/L occurred in 0.7% of Victoza®-treated patients, 0.3% of placebo-treated patients, and 0.5% of active-comparator-treated patients, with an incidence of 1.1% among patients treated with 1.8 mg/day of Victoza®. The clinical significance of these findings is unknown. Counsel patients regarding the risk for MTC and the symptoms of thyroid tumors (e.g. a mass in the neck, dysphagia, dyspnea or persistent hoarseness). It is unknown whether monitoring with serum calcitonin or thyroid ultrasound will mitigate the potential risk of MTC, and such monitoring may increase the risk of unnecessary procedures, due to low test specificity for serum calcitonin and a high background incidence of thyroid disease. Patients with thyroid nodules noted on physical examination or neck imaging obtained for other reasons should be referred to an endocrinologist for further evaluation. Although routine monitoring of serum calcitonin is of uncertain value in patients treated with Victoza®, if serum calcitonin is measured and found to be elevated, the patient should be referred to an endocrinologist for further evaluation. **Pancreatitis: Based on spontaneous postmarketing reports, acute pancreatitis, including fatal and non-fatal hemorrhagic or necrotizing pancreatitis, has been observed in patients treated with Victoza®. After initiation of Victoza®, observe patients carefully for signs and symptoms of pancreatitis (including persistent severe abdominal pain, sometimes radiating to the back and which may or may not be accompanied by vomiting). If pancreatitis is suspected, Victoza® should promptly be discontinued and appropriate management should be initiated. If pancreatitis is confirmed, Victoza® should not be restarted. Consider antidiabetic therapies other than Victoza® in patients with a history of pancreatitis.** In clinical trials of Victoza®, there have been 13 cases of pancreatitis among Victoza®-treated patients and 1 case in a comparator (glimepiride) treated patient (2.7 vs. 0.5 cases per 1000 patient-years). Nine of the 13 cases with Victoza® were reported as acute pancreatitis and four were reported as chronic pancreatitis. In one case in a Victoza®-treated patient, pancreatitis, with necrosis, was observed and led to death; however clinical causality could not be established. Some patients had other risk factors for pancreatitis, such as a history of cholelithiasis or alcohol abuse. **Use with Medications Known to Cause Hypoglycemia:** Patients receiving Victoza® in combination with an insulin secretagogue (e.g., sulfonylurea) or insulin may have an increased risk of hypoglycemia. The risk of hypoglycemia may be lowered by a reduction in the dose of sulfonylurea (or other concomitantly administered insulin secretagogues) or insulin **Renal Impairment:** Victoza® has not been found to be directly nephrotoxic in animal studies or clinical trials. There have been postmarketing reports of acute renal failure and worsening of chronic renal failure, which may sometimes require hemodialysis in Victoza®-treated patients. Some of these events were reported in patients without known underlying renal disease. A majority of the reported events occurred in patients who had experienced nausea, vomiting, diarrhea, or dehydration. Some of the reported events occurred in patients receiving one or more medications known to affect renal function or hydration status. Altered renal function has been reversed in many of the reported cases with supportive treatment and discontinuation of potentially causative agents, including Victoza®. Use caution when initiating or escalating doses of Victoza® in patients with renal impairment. **Hypersensitivity Reactions:** There have been postmarketing reports of serious hypersensitivity reactions (e.g., anaphylactic reactions and angioedema) in patients treated with Victoza®. If a hypersensitivity reaction occurs, the patient should discontinue Victoza® and other suspect medications and promptly seek medical advice. Angioedema has also been reported with other GLP-1 receptor agonists. Use caution in a patient with a history of angioedema with another GLP-1 receptor agonist because it is unknown whether such patients will be predisposed to angioedema with Victoza®. **Macrovascular Outcomes:** There have been no clinical studies establishing conclusive evidence of macrovascular risk reduction with Victoza® or any other antidiabetic drug.

**ADVERSE REACTIONS: Clinical Trials Experience:** Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice. The safety of Victoza® has been evaluated in 8 clinical trials: A double-blind 52-week monotherapy trial compared Victoza® 1.2 mg daily, Victoza® 1.8 mg daily, and glimepiride 8 mg daily; A double-blind 26 week add-on to metformin trial compared Victoza® 0.6 mg once-daily, Victoza® 1.2 mg once-daily, Victoza® 1.8 mg once-daily, placebo, and glimepiride 4 mg once-daily; A double-blind 26 week add-on to glimepiride trial compared Victoza® 0.6 mg daily, Victoza® 1.2 mg once-daily, Victoza® 1.8 mg once-daily, placebo, and rosiglitazone 4 mg once-daily; A 26 week add-on to metformin + glimepiride trial, compared double-blind Victoza® 1.8 mg once-daily, double-blind placebo, and open-label insulin glargine once-daily; A double-blind 26-week add-on to metformin + rosiglitazone trial compared Victoza® 1.2 mg once-daily, Victoza® 1.8 mg once-daily and placebo; An open-label 26-week add-on to metformin and/or sulfonylurea trial compared Victoza® 1.8 mg once-daily and exenatide 10 mcg twice-daily; An open-label 26-week add-on to metformin trial compared Victoza® 1.2 mg once-daily, Victoza® 1.8 mg once-daily, and sitagliptin 100 mg once-daily; An open-label 26-week trial compared insulin detemir as add-on to Victoza® 1.8 mg + metformin to continued treatment with Victoza® + metformin alone. *Withdrawals:* The incidence of withdrawal due to adverse events was 7.8% for Victoza®-treated patients and 3.4% for comparator-treated patients in the five double-blind controlled trials of 26 weeks duration or longer. This difference was driven by withdrawals due to gastrointestinal adverse reactions, which occurred in 5.0% of Victoza®-treated patients and 0.5% of comparator-treated patients. In these five trials, the most common adverse reactions leading to withdrawal for Victoza®-treated patients were nausea (2.8% versus 0% for comparator) and vomiting (1.5% versus 0.1% for comparator). Withdrawal due to gastrointestinal adverse events mainly occurred during the first 2-3 months of the trials. *Common adverse reactions:* Tables 1, 2, 3 and 4 summarize common adverse reactions (hypoglycemia is discussed separately) reported in seven of the eight controlled trials of 26 weeks duration or longer. Most of these adverse reactions were gastrointestinal in nature. In the five double-blind clinical trials of 26 weeks duration or longer, gastrointestinal adverse reactions were reported in 41% of Victoza®-treated patients and were dose-related. Gastrointestinal adverse reactions occurred in 17% of comparator-treated patients. Common adverse reactions that occurred at a higher incidence among Victoza®-treated patients included nausea, vomiting, diarrhea, dyspepsia and constipation. In the five double-blind and three open-label clinical trials of 26 weeks duration or longer, the percentage of patients who reported nausea declined over time. In the five double-blind trials approximately 13% of Victoza®-treated patients and 2% of comparator-treated patients reported nausea during the first 2 weeks of treatment. In the 26-week open-label trial comparing Victoza® to exenatide, both in combination with metformin and/or sulfonylurea, gastrointestinal adverse reactions were reported at a similar incidence in the Victoza® and exenatide treatment groups (Table 3). In the 26-week open-label trial comparing Victoza® 1.2 mg, Victoza® 1.8 mg and sitagliptin 100 mg, all in combination with metformin, gastrointestinal adverse reactions were reported at a higher incidence with Victoza® than sitagliptin (Table 4). In the remaining 26-week trial, all patients received Victoza® 1.8 mg + metformin during a 12-week run-in period. During the run-in period, 167 patients (17% of enrolled total) withdrew from the trial: 76 (46% of withdrawals) of these patients doing so because of gastrointestinal adverse reactions and 15 (9% of withdrawals) doing so due to other adverse events. Only those patients who completed the run-in period with inadequate glycemic control were randomized to 26 weeks of add-on therapy with insulin detemir or continued, unchanged treatment with Victoza® 1.8 mg + metformin. During this randomized 26-week period, diarrhea was the only adverse reaction reported in ≥5% of patients treated with Victoza® 1.8 mg + metformin + insulin detemir (11.7%) and greater than in patients treated with Victoza® 1.8 mg and metformin alone (6.9%).

**Table 1: Adverse reactions reported in ≥5% of Victoza®-treated patients in a 52-week monotherapy trial**

| | All Victoza® N = 497 | Glimepiride N = 248 |
|---|---|---|
| **Adverse Reaction** | (%) | (%) |
| Nausea | 28.4 | 8.5 |
| Diarrhea | 17.1 | 8.9 |
| Vomiting | 10.9 | 3.6 |
| Constipation | 9.9 | 4.8 |
| Headache | 9.1 | 9.3 |

**Table 2: Adverse reactions reported in ≥5% of Victoza®-treated patients and occurring more frequently with Victoza® compared to placebo: 26-week combination therapy trials**

| **Add-on to Metformin Trial** | | | |
|---|---|---|---|
| | All Victoza® + Metformin N = 724 | Placebo + Metformin N = 121 | Glimepiride + Metformin N = 242 |
| **Adverse Reaction** | (%) | (%) | (%) |
| Nausea | 15.2 | 4.1 | 3.3 |
| Diarrhea | 10.9 | 4.1 | 3.7 |
| Headache | 9.0 | 6.6 | 9.5 |
| Vomiting | 6.5 | 0.8 | 0.4 |
| **Add-on to Glimepiride Trial** | | | |
| | All Victoza® + Glimepiride N = 695 | Placebo + Glimepiride N = 114 | Rosiglitazone + Glimepiride N = 231 |
| **Adverse Reaction** | (%) | (%) | (%) |
| Nausea | 7.5 | 1.8 | 2.6 |
| Diarrhea | 7.2 | 1.8 | 2.2 |

| | | | |
|---|---|---|---|
| Constipation | 5.3 | 0.9 | 1.7 |
| Dyspepsia | 5.2 | 0.9 | 2.6 |
| **Add-on to Metformin + Glimepiride** | | | |
| | Victoza® 1.8 + Metformin + Glimepiride N = 230 | Placebo + Metformin + Glimepiride N = 114 | Glargine + Metformin + Glimepiride N = 232 |
| **Adverse Reaction** | (%) | (%) | (%) |
| Nausea | 13.9 | 3.5 | 1.3 |
| Diarrhea | 10.0 | 5.3 | 1.3 |
| Headache | 9.6 | 7.9 | 5.6 |
| Dyspepsia | 6.5 | 0.9 | 1.7 |
| Vomiting | 6.5 | 3.5 | 0.4 |
| **Add-on to Metformin + Rosiglitazone** | | | |
| | All Victoza® + Metformin + Rosiglitazone N = 355 | Placebo + Metformin + Rosiglitazone N = 175 | |
| **Adverse Reaction** | (%) | (%) | |
| Nausea | 34.6 | 8.6 | |
| Diarrhea | 14.1 | 6.3 | |
| Vomiting | 12.4 | 2.9 | |
| Headache | 8.2 | 4.6 | |
| Constipation | 5.1 | 1.1 | |

**Table 3: Adverse Reactions reported in ≥5% of Victoza®-treated patients in a 26-Week Open-Label Trial versus Exenatide**

| | **Victoza® 1.8 mg once daily + metformin and/or sulfonylurea** N = 235 | **Exenatide 10 mcg twice daily + metformin and/or sulfonylurea** N = 232 |
|---|---|---|
| **Adverse Reaction** | (%) | (%) |
| Nausea | 25.5 | 28.0 |
| Diarrhea | 12.3 | 12.1 |
| Headache | 8.9 | 10.3 |
| Dyspepsia | 8.9 | 4.7 |
| Vomiting | 6.0 | 9.9 |
| Constipation | 5.1 | 2.6 |

**Table 4: Adverse Reactions in ≥5% of Victoza®-treated patients in a 26-Week Open-Label Trial versus Sitagliptin**

| | **All Victoza® + metformin** N = 439 | **Sitagliptin 100 mg/day + metformin** N = 219 |
|---|---|---|
| **Adverse Reaction** | (%) | (%) |
| Nausea | 23.9 | 4.6 |
| Headache | 10.3 | 10.0 |
| Diarrhea | 9.3 | 4.6 |
| Vomiting | 8.7 | 4.1 |

*Immunogenicity:* Consistent with the potentially immunogenic properties of protein and peptide pharmaceuticals, patients treated with Victoza® may develop anti-liraglutide antibodies. Approximately 50-70% of Victoza®-treated patients in the five double-blind clinical trials of 26 weeks duration or longer were tested for the presence of anti-liraglutide antibodies at the end of treatment. Low titers (concentrations not requiring dilution of serum) of anti-liraglutide antibodies were detected in 8.6% of these Victoza®-treated patients. Sampling was not performed uniformly across all patients in the clinical trials, and this may have resulted in an underestimate of the actual percentage of patients who developed antibodies. Cross-reacting anti-liraglutide antibodies to native glucagon-like peptide-1 (GLP-1) occurred in 6.9% of the Victoza®-treated patients in the double-blind 52-week monotherapy trial and in 4.8% of the Victoza®-treated patients in the double-blind 26-week add-on combination therapy trials. These cross-reacting antibodies were not tested for neutralizing effect against native GLP-1, and thus the potential for clinically significant neutralization of native GLP-1 was not assessed. Antibodies that had a neutralizing effect on liraglutide in an *in vitro* assay occurred in 2.3% of the Victoza®-treated patients in the double-blind 52-week monotherapy trial and in 1.0% of the Victoza®-treated patients in the double-blind 26-week add-on combination therapy trials. Among Victoza®-treated patients who developed anti-liraglutide antibodies, the most common category of adverse events was that of infections, which occurred among 40% of these patients compared to 36%, 34% and 35% of antibody-negative Victoza®-treated, placebo-treated and active-control-treated patients, respectively. The specific infections which occurred with greater frequency among Victoza®-treated antibody-positive patients were primarily nonserious upper respiratory tract infections, which occurred among 11% of Victoza®-treated antibody-positive patients; and among 7%, 7% and 5% of antibody-negative Victoza®-treated, placebo-treated and active-control-treated patients, respectively. Among Victoza®-treated antibody-negative patients, the most common category of adverse events was that of gastrointestinal events, which occurred in 43%, 18% and 19% of antibody-negative Victoza®-treated, placebo-treated and active-control-treated patients, respectively. Antibody formation was not associated with reduced efficacy of Victoza® when comparing mean $HbA_{1c}$ of all antibody-positive and all antibody-negative patients. However, the 3 patients with the highest titers of anti-liraglutide antibodies had no reduction in $HbA_{1c}$ with Victoza® treatment. In the five double-blind clinical trials of Victoza®, events from a composite of adverse events potentially related to immunogenicity (e.g. urticaria, angioedema) occurred among 0.8% of Victoza®-treated patients and among 0.4% of comparator-treated patients. Urticaria accounted for approximately one-half of the events in this composite for Victoza®-treated patients. Patients who developed anti-liraglutide antibodies were not more likely to develop events from the immunogenicity events composite than were patients who did not develop anti-liraglutide antibodies. *Injection site reactions:* Injection site reactions (e.g., injection site rash, erythema) were reported in approximately 2% of Victoza®-treated patients in the five double-blind clinical trials of at least 26 weeks duration. Less than 0.2% of Victoza®-treated patients discontinued due to injection site reactions. *Papillary thyroid carcinoma:* In clinical trials of Victoza®, there were 7 reported cases of papillary thyroid carcinoma in patients treated with Victoza® and 1 case in a comparator-treated patient (1.5 vs. 0.5 cases per 1000 patient-years). Most of these papillary thyroid carcinomas were <1 cm in greatest diameter and were diagnosed in surgical pathology specimens after thyroidectomy prompted by findings on protocol-specified screening with serum calcitonin or thyroid ultrasound. *Hypoglycemia:* In the eight clinical trials of at least 26 weeks duration, hypoglycemia requiring the assistance of another person for treatment occurred in 11 Victoza®-treated patients (2.3 cases per 1000 patient-years) and in two exenatide-treated patients. Of these 11 Victoza®-treated patients, six patients were concomitantly using metformin and a sulfonylurea, one was concomitantly using a sulfonylurea, two were concomitantly using metformin (blood glucose values were 65 and 94 mg/dL) and two were using Victoza® as monotherapy (one of these patients was undergoing an intravenous glucose tolerance test and the other was receiving insulin as treatment during a hospital stay). For these two patients on Victoza® monotherapy, the insulin treatment was the likely explanation for the hypoglycemia. In the 26-week open-label trial comparing Victoza® to sitagliptin, the incidence of hypoglycemic events defined as symptoms accompanied by a fingerstick glucose <56 mg/dL was comparable among the treatment groups (approximately 5%).

**Table 5: Incidence (%) and Rate (episodes/patient year) of Hypoglycemia in the 52-Week Monotherapy Trial and in the 26-Week Combination Therapy Trials**

| | **Victoza® Treatment** | **Active Comparator** | **Placebo Comparator** |
|---|---|---|---|
| **Monotherapy** | **Victoza®** (N = 497) | **Glimepiride** (N = 248) | **None** |
| Patient not able to self–treat | 0 | 0 | — |
| Patient able to self–treat | 9.7 (0.24) | 25.0 (1.66) | — |
| Not classified | 1.2 (0.03) | 2.4 (0.04) | — |
| **Add-on to Metformin** | **Victoza® + Metformin** (N = 724) | **Glimepiride + Metformin** (N = 242) | **Placebo + Metformin** (N = 121) |
| Patient not able to self–treat | 0.1 (0.001) | 0 | 0 |
| Patient able to self–treat | 3.6 (0.05) | 22.3 (0.87) | 2.5 (0.06) |
| **Add-on to Victoza® + Metformin** | **Insulin detemir + Victoza® + Metformin** (N = 163) | **Continued Victoza® + Metformin alone** (N = 158*) | **None** |
| Patient not able to self–treat | 0 | 0 | — |
| Patient able to self–treat | 9.2 (0.29) | 1.3 (0.03) | — |
| **Add-on to Glimepiride** | **Victoza® + Glimepiride** (N = 695) | **Rosiglitazone + Glimepiride** (N = 231) | **Placebo + Glimepiride** (N = 114) |
| Patient not able to self–treat | 0.1 (0.003) | 0 | 0 |
| Patient able to self–treat | 7.5 (0.38) | 4.3 (0.12) | 2.6 (0.17) |
| Not classified | 0.9 (0.05) | 0.9 (0.02) | 0 |
| **Add-on to Metformin + Rosiglitazone** | **Victoza® + Metformin + Rosiglitazone** (N = 355) | **None** | **Placebo + Metformin + Rosiglitazone** (N = 175) |
| Patient not able to self–treat | 0 | — | 0 |
| Patient able to self–treat | 7.9 (0.49) | — | 4.6 (0.15) |
| Not classified | 0.6 (0.01) | — | 1.1 (0.03) |
| **Add-on to Metformin + Glimepiride** | **Victoza® + Metformin + Glimepiride** (N = 230) | **Insulin glargine + Metformin + Glimepiride** (N = 232) | **Placebo + Metformin + Glimepiride** (N = 114) |
| Patient not able to self–treat | 2.2 (0.06) | 0 | 0 |
| Patient able to self–treat | 27.4 (1.16) | 28.9 (1.29) | 16.7 (0.95) |
| Not classified | 0 | 1.7 (0.04) | 0 |

*One patient is an outlier and was excluded due to 25 hypoglycemic episodes that the patient was able to self-treat. This patient had a history of frequent hypoglycemia prior to the study.

In a pooled analysis of clinical trials, the incidence rate (per 1,000 patient-years) for malignant neoplasms (based on investigator-reported events, medical history, pathology reports, and surgical reports from both blinded and open-label study periods) was 10.9 for Victoza®, 6.3 for placebo, and 7.2 for active comparator. After excluding papillary thyroid carcinoma events *[see Adverse Reactions]*, no particular cancer cell type predominated. Seven malignant neoplasm events were reported beyond 1 year of exposure to study medication, six events among Victoza®-treated patients (4 colon, 1 prostate and 1 nasopharyngeal), no events with placebo and one event with active comparator (colon). Causality has not been established. **Laboratory Tests:** In the five clinical trials of at least 26 weeks duration, mildly elevated serum bilirubin concentrations (elevations to no more than twice the upper limit of the reference range) occurred in 4.0% of Victoza®-treated patients, 2.1% of placebo-treated patients and 3.5% of active-comparator-treated patients. This finding was not accompanied by abnormalities in other liver tests. The significance of this isolated finding is unknown. **Vital signs:** Victoza® did not have adverse effects on blood pressure. Mean increases from baseline in heart rate of 2 to 3 beats per minute have been observed with Victoza® compared to placebo. The long-term clinical effects of the increase in pulse rate have not been established. **Post-Marketing Experience:** The following additional adverse reactions have been reported during post-approval use of Victoza®. Because these events are reported voluntarily from a population of uncertain size, it is generally not possible to reliably estimate their frequency or establish a causal relationship to drug exposure: Dehydration resulting from nausea, vomiting and diarrhea; Increased serum creatinine, acute renal failure or worsening of chronic renal failure, sometimes requiring hemodialysis; Angioedema and anaphylactic reactions; Allergic reactions: rash and pruritus; Acute pancreatitis, hemorrhagic and necrotizing pancreatitis sometimes resulting in death.

**OVERDOSAGE:** Overdoses have been reported in clinical trials and post-marketing use of Victoza®. Effects have included severe nausea and severe vomiting. In the event of overdosage, appropriate supportive treatment should be initiated according to the patient's clinical signs and symptoms.

**More detailed information is available upon request.**

For information about Victoza® contact: Novo Nordisk Inc., 800 Scudders Mill Road, Plainsboro, NJ 08536, 1–877-484-2869

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novo nordisk®

VICTOZA®

liraglutide (rDNA origin) injection

# High Tech Health Care

John J. Frey III, MD, Medical Editor

For those of us whose experience with technology early in our careers consisted of spinning hematocrits in fragile, breakable tubes and looking at spun urines for sediment, the diagnostic technologies today are still a bit of a dazzle. Those early experiences created a healthy skepticism about the added value of each "new thing." My teacher's voice asking, "So, will this test make you more certain or will it lead to more tests?" still rings in my head.

Research in technology assessment is notoriously post hoc. Teaching someone how to use a new technology—whether robotic surgery or, in the study by Wong and colleagues in this issue of the *WMJ,* teaching residents to use hand-held ultrasound[1]—often takes priority over comparing the value of that technology to what already exists. For example, do ultrasounds or CT scans improve the assessment of the risk of appendicitis over the increasingly lost art of physical examination of the patient? Is the cost worth it?

It has been known for decades that the presence of a technology increases the likelihood of its use, but the effects on care can be negative.[2] If we can get by the problems of identity and control that a technology almost always raises, we need to study the effects of its use in patient care. If a hand-held ultrasound can save time, improve diagnostic accuracy, decrease cost, and be subjected to quality assurance in the hands of the operator, then it should become part of the armamentarium of clinicians. That research, however, remains to be done.

The potential exists for social media to be used for everything from virtual grouping of patients sharing experiences and education on social networks to the epidemiology of infectious diseases by looking for an increase in terms in common social media.[3] Moreno and her colleagues[4] looked at college students who displayed the term for a local block party on their Facebook pages and compared them to a cohort who attended the party but did not display, and found that displaying the party was associated with a much higher level of drinking at the event. They use these findings to suggest that advertising directed against binge drinking stimulated by the mention of an event highly correlated with drinking might, for example, be put on Facebook. At first one wonders how that could be done, but the next time you travel and read a newspaper online and see advertisements geared to the location where you are reading it, realize that the same could be done with warnings about high-risk behavior in lots of situations. The possibilities, just like the ads, seem endless.

A scale is a much simpler technology and available everywhere. So, ask Boyle and Boyle,[5] why do we ignore it so often when we prescribe antibiotics for adults? They use a chart review of rhinosinusitis as a proxy to look at weight-adjusted dosing for antibiotics and find, perhaps to no one's surprise, that there are no adjustments. We spend a great deal of time carefully looking at weight-adjusted dosing for children but, they ask, why does that need disappear above a certain age? If anything, with the widely acknowledged increase in adult obesity in the country, why do we treat everyone as if they are the "standard 70 kilogram man" that represented the "average" in textbooks from 40 years ago? I am not sure when I last actually saw a 70 kilogram man.

It has been known for decades that the presence of a technology increases the likelihood of its use, but the effects on care can be negative. If we can get by the problems of identity and control that a technology almost always raises, we need to study the effects of its use in patient care.

Kasirye and colleagues'[6] study of the predictive value of blood glucose on hospitalized patients with COPD represents an important way of identifying patients who are more likely to have higher levels of morbidity, longer length of stay, and be at greater risk of dying. It would be safe to say that all patients admitted to hospitals get glucose as part of their admission panels. While clinicians might emphasize controlling elevated blood sugars in patients, this study in a population of patients with identified pulmonary disease shows that we should be alerted to patients with low blood sugars as high risk and offer more aggressive monitoring and treatment. The work by Kasirye and colleagues needs to be expanded to other populations of hospital-

ized patients, but represents an important and widely available marker for patients who need closer and more intensive care. The standardization of treatment is important in areas such as prevention of hospital-acquired infections, but it is the individualization of patients into higher or lower risk groups that often is the greatest challenge. This study offers one simple method of doing so.

An odd tumor in an odd place is the lesson from the case study of Subramanian and colleagues.[7] Case reports are always reminders that zebras do in fact exist, and when one spots one it is good to tell others.

Finally, on behalf of the *WMJ* Editorial Board and staff, I'd like to thank everyone who served as a reviewer this year. In addition to being an important collegial act, manuscript review is essential to the integrity of *WMJ*. A complete list of reviewers and information about joining this group is on page 265 in this issue.

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# Examination of Antibiotic Dosing Practices for Refractory Rhinosinusitis in Relation to Body Weight

Timothy R. Boyle, MD, FACS; Emmalee A. Boyle


## ABSTRACT

**Objective:** Rhinosinusitis is a common condition that is frequently treated as an infectious disease with antibiotics. In general, antibiotic dosing in adults follows a flat scheme with no regard for body size. Wide variability in body weight raises concern whether this dosing scheme results in efficacious dosing for patients of various sizes. If not, larger patients with chronic rhinosinusitis may have avoidable morbidity from their disease, and surgery may be prematurely recommended. Our goal was to better understand the possible treatment implications of varying body size when prescribing antibiotics for chronic rhinosinusitis.

**Design:** Retrospective chart review.

**Setting:** Otolaryngology referral center at a multispecialty medical center.

**Participants:** Patients (N=180) with refractory chronic rhinosinusitis referred to an otolaryngologist for consideration of sinus surgery.

**Methods:** Main outcome measures included antibiotic usage, dosing, and body size metrics.

**Results:** There was wide variation in patient weight and body mass index. However, treatment guidelines for adults do not recommend dosage adjustments for variation in weight, and there was little variation in dosing strategies for each antibiotic prescribed. Therefore, per kilogram dosing varied widely between patients. Of the 9 antibiotics prescribed for chronic rhinosinusitis, the median per kilogram dose of only 1 antibiotic exceeded the minimum recommended per kilogram dose for children.

**Conclusion:** In the absence of weight-based guidelines for antibiotic administration, the potential for suboptimal dosing in patients seeking relief for chronic rhinosinusitis or other infectious diseases is great, and further study is needed to examine dosing practices.


## INTRODUCTION

Rhinosinusitis is a common medical condition that affects as many as 14% of adults in the United States each year[1] and generally is treated in practice as an infectious disease. Chronic rhinosinusitis is defined as rhinosinusitis that persists for 12 weeks or longer without resolution.[2] Following acute rhinosinusitis, chronic rhinosinusitis develops within 4 years in approximately 5.5% of patients.[1] The pathophysiology of chronic rhinosinusitis is not well-defined, but it is generally accepted to be an inflammatory disease in which bacterial colonization may contribute to pathogenesis.[3] In the United States, the cost of disease management for chronic rhinosinusitis is estimated to be between $4.3 billion and $5.8 billion per year,[4,5] with the average patient spending nearly $2500 on disease management, including antibiotics, in the year preceding endoscopic sinus surgery.[1] There are currently no FDA-approved antibiotics for the treatment of chronic rhinosinusitis and in a 2011 Cochrane review, Piromchai et al[6] found only 1 randomized controlled trial examining the efficacy of antibiotic treatment for chronic rhinosinusitis. Based on lack of strong evidence, current guidelines recommend antibiotics as an option for the treatment of chronic rhinosinusitis in conjunction with other steroidal or decongestant therapies.[3,7] Regardless, antibiotics frequently are prescribed.[8] It is estimated that 94% of otolaryngologists in the United States prescribe prolonged courses of oral antibiotics for the treatment of chronic rhinosinusitis,[9] and that more than 1 in 5 antibiotics prescribed in adults are for rhinosinusitis.[10] Dosing strategies are based on standard guidelines with modification for relevant disease, perceived severity, and recent antibiotic use.[10,11] However, while dosing varies with body size in children up to 40 kg, there are no accepted recommendations for varying dose in relation to body size in adults. Adults who weight 70 kg are routinely prescribed the same dose as those who weight 150 kg.

The influence of body size on drug distribution is well-recognized. Body size is an important consideration for optimizing drug therapy in pediatrics, hematology, oncology, anesthesia and critical care, and evidence suggests that the physiological

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**Table 1.** Patient Demographics (N = 180)

| **Gender** | **n (%)** |
|---|---|
| Male | 85 (47.2) |
| Female | 95 (52.8) |
| **Median age (range)** | |
| Male | 53 (21 – 83) |
| Female | 53 (21 – 88) |
| **Median body weight (range)** | |
| Male (kg) | 92 (55.1 – 160) |
| Female (kg) | 77 (45 – 126) |
| **Median body mass index (BMI) (range)** | |
| Male | 29.1 (18.8 – 47.6) |
| Female | 28.6 (16.7 – 45) |
| **Obese (BMI ≥ 30), n (%)** | |
| Male | 36 (42.3) |
| Female | 40 (42.1) |

changes associated with obesity can alter important pharmacokinetic properties, including distribution and clearance.[12] However, body size is not considered in dosing for antimicrobial therapy in adults.[13] In general, pharmacodynamics studies are lacking for antibiotic use in adult patients of varying body size, and it is unknown whether equal dosing in patients with widely variable weights or body compositions is equally efficacious, although there is some evidence to the contrary.[12] In the case of chronic rhinosinusitis, suboptimal dosing may mean avoidable morbidity and the premature recommendation for surgical intervention. This study was designed to review antibiotic choices and dosing regimens before referral for evaluation of surgical treatment for refractory rhinosinusitis and to consider the possible treatment implications of varying body size among our patient population.

## METHODS

This study was performed in the Department of Otolaryngology at Marshfield Clinic, a large, multispecialty group practice located in central Wisconsin. It was approved by the Marshfield Clinic Research Foundation Institutional Review Board. A retrospective review was performed on the electronic medical record (EMR) of adults aged 19 years and older who were referred by their primary medical provider to a single otolaryngologist for surgical treatment of refractory rhinosinusitis between January 2006 and June 2009. All patients were considered to have failed antibiotic and other "maximal" medical therapy including nasal steroids, systemic steroids, antihistamines, and saline irrigations. Upon referral, nearly all patients considered themselves to have chronic sinusitis and met symptom length criteria; however, many were not formally designated as such. Study subjects underwent a detailed otolaryngic evaluation including endoscopic examination of the nose and/or computed tomography scan of the sinuses. All patient physical examination and radiographic data were retrieved from the Marshfield Clinic EMR. Age, sex, symptoms, ear, nose and throat examination findings, antibiotic and dosage, weight, body mass index, radiographic results, and surgical intervention were recorded. Patients with primary noninfectious diagnoses including nasal polyps, allergic rhinitis, tumors, or septal obstructions were excluded. Patients with cystic fibrosis or allergic fungal sinusitis also were excluded.

Recommended dosing strategies for all antibiotics examined were obtained from the Physicians' Desk Reference (PDR) Network.[14] Recommended doses for amoxicillin-clavulanate, levofloxacin, azithromycin, ciprofloxacin, and clarithromycin are specific for acute bacterial rhinosinusitis. The recommended dose of amoxicillin is for infections of the ear, nose, and throat. The recommended dose of cephalexin is described as the "usual" amount. The recommended dose of trimethoprim-sulfamethoxazole is the standard dose recommended for other indications, and that for clindamycin is the standard dose for "serious infection." Because adult dosing, unlike pediatric dosing, is flat and not based on weight, the per kg dose recommended for children weighing less than 40 kg was used as a weight-based comparator for the purposes of this study. The primary analyses in this report are descriptive and based on standard summary statistics.

## RESULTS

Between January 2006 and July 2009, 180 (47.2% male) patients met inclusion criteria for chart review (Table 1). All patients had been treated multiple times for sinusitis, although few were specifically designated as "chronic" by their primary care providers. All patients received multiple courses of antibiotics. The most recent antibiotic course likely would have been chosen considering the environment of recent antibiotic use and a higher likelihood of resistant organisms.

All patients were referred to the otolaryngologist in the midst of a course of or immediately after completing a course of antibiotics. Antibiotic therapy used at the time of referral is shown in Table 2. The most frequently prescribed antibiotic was amoxicillin-clavulanate (37.8%), followed by levofloxacin (18.3%), azithromycin (16.1%), and amoxicillin (12.2%). Cephalexin, clarithromycin, trimethoprim-sulfamethoxazole, and clindamycin were each prescribed to 5% of patients or fewer. Antibiotic dosing was relatively consistent. For each antibiotic, the majority of patients received the same daily dose. Adult dosing recommendations for the antibiotics commonly prescribed for rhinosinusitis were obtained from the PDR Network[14] and are also shown in Table 2. The median daily dose coincided with PDR Network guidelines for levofloxacin, ciprofloxacin, clarithromycin, and trimethoprim-sulfamethoxazole, but was higher for amoxicillin-clavulanate, amoxicillin, and cephalexin and lower for azithromycin and clindamycin (Table 3).

Patient body weight varied widely, resulting in large variation in the median per kilogram dose prescribed for each antibiotic (Table 4). Based on body weight, few patients received what would be considered the minimum therapeutic dose in

children. The median per kilogram dose was less than the recommended pediatric per kilogram dose for all but one of the antibiotics examined (Table 4). There was no evidence of any patient receiving a larger dose of a previously prescribed antibiotic. All patients either received the doses described or lower doses of the same or other antibiotics in previous treatment failures.

## DISCUSSION

Acute and chronic rhinosinusitis are conditions that are commonly diagnosed and treated.[1] When acute bacterial rhinosinusitis is suspected, antibiotics generally are administered in order to return the sinuses to health, decrease symptom duration, prevent severe complications, and decrease development of chronic disease.[11] Many studies have demonstrated significant clinical benefit from the use of antibiotics in acute bacterial rhinosinusitis.[15] The efficacy of antibiotics in chronic rhinosinusitis is unclear,[15] and no antibiotic is currently FDA-approved for the treatment of chronic sinusitis, although they are routinely prescribed.[8,9]

Adequate antibiotic dosing for chronic rhinosinusitis is unclear and difficult to define. Even some antibiotics that are commonly used for acute bacterial sinusitis have no approved indication in their literature, including cephalexin, trimethoprim-sulfamethoxazole, and clindamycin. Antibiotic efficacy is dependent on several factors, including antibiotic chosen, dose and duration of antibiotic therapy, and appropriate diagnosis.[15] Dosing for these antibiotics tends to follow otitis media guidelines. For previously untreated patients, standard dose amoxicillin is recommended as a first line antibiotic intervention.[10] *The Physicians' Desk Reference* recommends amoxicillin for infections caused by susceptible (β-lactamase negative) strains of *Streptococcus pneumoniae, Staphylococcus* spp., or *Haemophilus influenzae,*[16] which account for approximately 40% to 90% of acute bacterial rhinosinusitis cases in adults.[11] There is no specific mention of *Moraxella catarrhalis*, which accounts for an additional 2% to 10% of cases in adults.[11] Adult dosing is recommended for children weighing more than 40 kg.[14] In the amoxicillin-treated group, patient weights ranged from 69 kg to 128 kg, but following the flat dosing scheme, the majority of patients were treated with 1500 mg per day, resulting in a wide range of per kilogram doses. All of these patients, whether

**Table 2.** Antibiotic Use and Dosing

| Antibiotic | N (%) | Recommended Daily Dose (mg)[14] | Median Daily Dose (mg) (range) | Received Median Daily Dose, n (%) |
|---|---|---|---|---|
| Amoxicillin-clavulanate | 68 (37.8) | 1000[a] | 1750 (1000 – 1750) | 59 (86.8) |
| Levofloxacin | 33 (18.3) | 500[a] | 500 (250 – 750) | 26 (78.8) |
| Azithromycin | 29 (16.1) | 500[a] | 250 (250 – 500) | 25 (86.2) |
| Amoxicillin | 22 (12.2) | 1000[b] | 1500 (500 – 3000) | 15 (68.2) |
| Ciprofloxacin | 9 (5.0) | 1000[a] | 1000 (500 – 1000) | 8 (88.9) |
| Cephalexin | 7 (3.9) | 1000[c] | 2000 (1500 – 2000) | 6 (85.7) |
| Clarithromycin | 6 (3.8) | 1000[a] | 1000 (1000 – 1000) | 6 (100.0) |
| Trimethoprim-sulfamethoxazole | 5 (2.8) | 320[d] | 320 (160 – 320) | 4 (80.0) |
| Clindamycin | 1 (0.6) | 1200[e] | 900 | 1 |

[a] Physician's desk reference (PDR)-recommended dose for acute bacterial rhinosinusitis.
[b]PDR-recommended dose for infections of the ear, nose, and throat.
[c]PDR-recommended "usual" amount.
[d]PDR-recommended amount for other indications.
[e]PDR-recommended dose for "serious infection."

**Table 3.** Recommended and Actual Antibiotic Dosing

| Antibiotic | N (%) | Recommended Regimen | Recommended Daily Dose (mg)[14] | Median Daily Dose (mg) (range) |
|---|---|---|---|---|
| Amoxicillin-clavulanate | 68 (37.8) | 500 mg q12h | 1000[a] | 1750 (1000 – 1750) |
| Levofloxacin | 33 (18.3) | 500 mg qd | 500[a] | 500 (250 – 750) |
| Azithromycin | 29 (16.1) | 500 mg qd | 500[a] | 250 (250 – 500) |
| Amoxicillin | 22 (12.2) | 500 mg q12h | 1000[b] | 1500 (500 – 3000) |
| Ciprofloxacin | 9 (5.0) | 500 mg q12h | 1000[a] | 1000 (500 – 1000) |
| Cephalexin | 7 (3.9) | 500 mg q12h | 1000[c] | 2000 (1500 – 2000) |
| Clarithromycin | 6 (3.8) | 500 mg q12h | 1000[a] | 1000 (1000 – 1000) |
| Trimethoprim-sulfamethoxazole | 5 (2.8) | 160 mg q12h | 320[d] | 320 (160 – 320) |
| Clindamycin | 1 (0.6) | 600 mg q12h | 1200[e] | 900 |

[a]PDR-recommended dose for acute bacterial rhinosinusitis.
[b]PDR-recommended dose for infections of the ear, nose, and throat.
[c]PDR-recommended "usual" amount.
[d]PDR-recommended amount for other indications.
[e]PDR-recommended dose for "serious infection."

**Table 4.** Per Kilogram Antibiotic Dosing

| Antibiotic | N (%) | Median Body Weight (kg) (range) | Median Per Kilogram Dose (mg/kg) (range) | Pediatric Minimum Therapeutic Dose (mg/kg)[a] |
|---|---|---|---|---|
| Amoxicillin-clavulanate | 68 (37.8) | 86 (58 – 126) | 19.3 (10.4 – 30.2) | 30 |
| Levofloxacin | 33 (18.3) | 81 (47 – 160) | 6.2 (3.1 – 13.9) | 8 |
| Azithromycin | 29 (16.1) | 83 (45 – 128) | 3.0 (1.9 – 8.5) | 10 |
| Amoxicillin | 22 (12.2) | 89 (48 – 128) | 16.9 (10.4 – 34.1) | 30 |
| Ciprofloxacin | 9 (5.0) | 88 (46 – 108) | 11.4 (5.4 – 21.7) | 10 |
| Cephalexin | 7 (3.9) | 108 (57 – 122) | 18.5 (16.4 – 35.1) | 25 |
| Clarithromycin | 6 (3.8) | 84 (79 – 86) | 11.9 (11.6 – 12.7) | 15 |
| Trimethoprim-sulfamethoxazole | 5 (2.8) | 84 (55 – 87) | 3.8 (2.0 – 5.8) | 8 |
| Clindamycin | 1 (0.6) | 108 | 8.3 | 16 |

[a]PDR-recommended per kg dose for children weighing less than 40 kg.[14]

they received the minimum 10.4 mg/kg dose or the maximum 34.1 mg/kg dose, were considered treatment failures upon referral to otolaryngology. However, many may not have received a therapeutic dose, as only one of the 22 patients who received amoxicillin was dosed at a level higher than the 30 mg/kg recommended in pediatric populations. Findings were similar for most of the antibiotics examined (Table 4).

The activity of most antibiotics ultimately depends on concentration at the site of infection; in this case, the sinus cavity. β-lactam antibiotics, such as amoxicillin, are time-dependent killers, and bacterial eradication is dependent on maintenance of concentrations at the site of infection above the minimum inhibitory concentration (MIC) of the organism for as much of the dosing period as possible.[11] The activity of macrolides, such as azithromycin, are similar except that these antibiotics exhibit persistent activity, and thus, effective bacterial eradication is dependent on the ratio of the antibiotic concentration at the site of infection over to MIC.[11] Fluoroquinolones, such as levofloxacin, are concentration-dependent killers, functioning best when concentrations are appreciably above the MIC of the pathogen, and dosing regimens are designed to maximize drug concentration at the site of infection.[11] Thus, in order to optimize efficacy, antibiotic concentrations at the site of infection must be maintained above the bacterial MIC for as long as possible during the antibiotic regimen.

Despite the high frequency of obesity in the United States,[17] few studies have examined drug distribution in obese patients, and even nonobese adults vary widely in body size and composition.[12,18] Several physiological changes occur in obesity that can alter pharmacodynamics by altering the processes of distribution, protein binding, metabolism, and clearance of antimicrobial agents.[13] While drug absorption does not appear to be altered in obesity, drug distribution into the tissue can be altered by body composition, regional blood flow, drug lipophilicity, and plasma protein binding.[12] Obesity also has been shown to alter glomerular filtration rate (GFR), which can affect clearance of antibiotics through the kidney.[12] Available data suggest that many antimicrobial agents, including β-lactams, vancomycin, fluoroquinolones, macrolides, linezolid, sulphonamides, and fluconazole, should be given in higher doses to patients with larger body size.[12] However, alteration of dose based on body weight is highly dependent on antibiotic of interest and in a 2000 review of the literature, Cheymol[18] noted major differences in determining appropriate dosages of vancomycin, ciprofloxacin, aminoglycosides, and gentamicin in morbidly obese patients. Conducting pharmacokinetic studies in subjects of varying size and composition is challenging, and while some progress has been made,[19,20] there is still no clear answer as to which size descriptor is best for studying pharmacokinetics in obese subjects.[18,21]

## CONCLUSION

Despite wide variability of body size and composition among adults and the tremendous increase in obesity in the past 30 years,[22] adult antibiotic recommendations are not based upon body weight or composition. Appropriate dosing of antibiotics not only improves drug efficacy, but also may reduce risk for the development of antimicrobial resistance.[17] As most antibiotics routinely prescribed for the treatment of rhinosinusitis are administered to adults as flat dosing regimens, we question whether it is reasonable to expect curative doses in patients of larger size. The data presented here demonstrate that there is wide variation in per kilogram dosing among chronic rhinosinusitis sufferers referred to an otolaryngologist, and that very few patients are treated at the per kilogram levels considered therapeutic in pediatric patients. We hypothesize that basing antibiotic administration on a flat dosing regimen without regard for body size or composition could result in misdosing, significantly affecting treatment outcome. Treatment with a nontherapeutic dose of antibiotics may result in treatment failure for patients with chronic rhinosinusitis, leading to unnecessary morbidity and premature referral for surgery.

The retrospective design of the present study is a major limitation. Although antibiotic therapy was used for the treatment of chronic rhinosinusitis in all cases, it is unlikely that antibiotic therapy was provided as the sole therapy, and the role of prescribed or over-the-counter steroidal or decongestant therapies was not examined. Future prospective studies should be designed to sample antibiotic concentrations in the blood and/or at the site of infection and determine bacterial MICs from sinus cultures in patients with different body sizes to determine whether suboptimal antibiotic dosing truly occurs in larger individuals with chronic rhinosinusitis. Additionally, future antibiotic pharmacodynamics studies should stratify by body size or take per kilogram dosing into account to evaluate the efficacy of flat versus variable dosing strategies in adults.

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# Association Between Blood Glucose Level and Outcomes in Patients Hospitalized for Acute Exacerbation of Chronic Obstructive Pulmonary Disease

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## ABSTRACT

**Background:** Increased blood glucose is associated with adverse clinical outcomes among patients with major illnesses. This study examined the association between blood glucose and adverse outcomes among hospitalized patients with acute exacerbation of chronic obstructive pulmonary disease, for which limited prior data were available.

**Methods:** We studied a cohort of 209 hospitalized patients with acute exacerbation of chronic obstructive pulmonary disease. Univariate analyses and multivariate logistic regression analyses with backward elimination method were performed to evaluate factors associated with in-hospital complications, length of hospitalization, 30-day hospital readmission, and 90-day all-cause mortality.

**Results:** Multivariate logistic regression analysis with backward elimination method revealed that lower blood glucose and age at hospital admission were the most significant risk factors for in-hospital complication. Received respiratory support and in-hospital complications were the most significant risk factors for the length of hospitalization. There were no significant risk factors associated with 30-day hospital readmission and 90-day all-cause mortality.

**Conclusion:** The analyses failed to reveal significant associations between higher blood glucose levels and adverse outcomes. We showed that lower glucose levels (hypoglycemia) results in higher risk for in-hospital complications. In-hospital complications results in longer length of hospitalization, which implies that lower glucose levels (hypoglycemia) indirectly may result in longer length of hospitalization. More studies are needed to better clarify the cause for these associations.

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## INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a condition affecting 24 million people and is the fourth leading cause of death in the United States,[1] with in-hospital mortality ranging from 2% to 30%.[2] Identification of prognostic factors may lead to improved treatment strategies and clinical outcomes for COPD. Among acute exacerbation of COPD (AECOPD) patients, adverse outcomes are associated with lower arterial pH, older age,[2-5] male gender, underlying comorbidities, higher income,[2,4,5] disease severity, and in-hospital complications.[5]

One readily available prognostic indicator is blood glucose. Data show that higher blood glucose is associated with adverse outcomes among patients with acute myocardial infarction,[6,7] brain injury,[8] community-acquired pneumonia,[9,10] severe trauma,[11] critical illness,[12-14] and those undergoing cardiothoracic surgery.[15-17] These results, along with the fact that nearly half of patients hospitalized with AECOPD suffer from hyperglycemia during hospitalization,[18,19] suggest that blood glucose could serve as an important tool for patient monitoring during AECOPD hospitalization. Studies have shown that hospitalized COPD patients with elevated blood glucose have longer hospital stays,[20] more frequent isolation of gram negative bacteria,[21] late non-invasive ventilatory failure,[22] and higher mortality risk.[23]

The association between hyperglycemia and AECOPD outcomes has not been fully described. Baker et al[18] reported a 15% increase in absolute risk of adverse outcomes for each 1 mol/l increase in blood glucose; however, the case definition used created the potential for inclusion of patients with conditions in

**Table 1.** Serum Glucose Measurements (Capillary and Serum) During Hospitalization

| Number of Blood Glucose Measurements Taken in a 24-hour Period | N | Mean | Median | Standard Deviation | Minimum | Maximum |
|---|---|---|---|---|---|---|
| 1 | 97 | 132 | 133 | 38 | 54 | 252 |
| 2 | 19 | 191 | 183 | 69 | 98 | 364 |
| 3 | 10 | 205 | 209 | 66 | 114 | 312 |
| 4 | 28 | 218 | 205 | 75 | 121 | 427 |
| 5 | 43 | 273 | 265 | 77 | 162 | 483 |
| 6 | 8 | 380 | 398 | 121 | 223 | 560 |
| 7 | 3 | 360 | 373 | 63 | 291 | 415 |
| 8 | 4 | 534 | 528 | 51 | 478 | 600 |
| 9 or more | 3 | 283 | 292 | 45 | 234 | 322 |

addition to AECOPD, such as bronchial asthma and pneumonia. Also, the authors' limited analysis to the highest value occurring at any time during the hospitalization[18] allows inference to be drawn from the absolute peak blood glucose value, but not from a complete picture of blood glucose during hospitalization.

The purpose of this study was to explore the association between blood glucose levels and clinical outcomes among hospitalized AECOPD patients on a general medical floor. We hypothesized that abnormal blood glucose (hypoglycemia and hyperglycemia) would be associated with adverse clinical outcomes.

## METHODS

### Study Population

A retrospective cohort of 209 patients hospitalized with a diagnosis of AECOPD within the Marshfield Epidemiology Surveillance Area (MESA), a 24-ZIP code area in central and northwestern Wisconsin,[24,25] were identified. Following institutional review board approval (with waiver of informed consent), patients were validated manually as meeting the study's inclusion criteria. Details about MESA are published elsewhere,[24,25] but briefly, this cohort consists of about 85,000 residents who receive health care at Marshfield Clinic and its affiliates. Patients had been admitted to the largest 2 hospitals in the MESA catchment area with a diagnosis of AECOPD from January 1, 2004 to December 31, 2008. Each patient was identified using ICD-9 Code 491.21 and a prehospitalization diagnosis of COPD based on the Global Initiative for Chronic Obstructive Lung Disease (GOLD) criteria,[26,27] which included (1) age 40–80 years; (2) history of smoking (>20 pack-years); (3) clinical history of COPD as measured at any time by an $FEV_1$/FVC ($FEV_1$ = forced expiratory volume in the first second of expiration/FVC = forced vital capacity) ratio <70% and $FEV_1$ <50% predicted. Inclusion criteria also included admission and discharge diagnosis of AECOPD and at least 2 blood glucose measurements during hospitalization. We excluded patients who were transferred from other facilities or those who were transferred to palliative or intensive care units within 24 hours of admission, newly diagnosed with lung cancer or pneumonia during the hospitalization, known to be HIV positive prior to admission, and those who left against medical advice. For patients with multiple admissions, the first admission was used. Data were obtained through electronic interrogation of the MESA database and manual chart abstraction.

### Data Collection

Demographic and clinical data collected for all subjects included age, gender, spirometry results, arterial blood gas on admission, body mass index (BMI), smoking history, comorbid conditions (identified in the Charlson Comorbidity Index[28]), use of noninvasive ventilation, plasma and serum blood glucose levels throughout the hospitalization, corticosteroid use with total daily dose (intravenous or oral), management of hyperglycemia (eg, diet, oral agents, insulin), and hospital discharge for reasons other than AECOPD within 30 days after the index hospital admission date.

Medical complications were extracted manually by review of patients' discharge summaries, and were defined as health care-associated infections (bacteremia, pneumonia, systemic inflammatory response syndrome), neurological (delirium, cerebrovascular accidents, coma), cardiac (new onset atrial fibrillation, decompensated congestive heart failure, myocardial infarction), or renal (acute renal failure defined as a rise in serum creatinine of at least 0.5 mg/dL over 24 hours). Serum glucose measurements (capillary and serum) measured during hospitalization were obtained (Table 1). For each patient, a daily mean blood glucose value was calculated from all measurements (fasting and random) done during hospitalization. Random blood glucose measurements were taken using a portable glucometer; fasting blood glucose was measured by Siemens Chemistry analyzer (Dimesions Xpand and Dimension EXL200 models) using a spectrophotometric hexokinase method. Daily mean blood glucose was expressed in milligrams per deciliter (mg/dL).

### Statistical Analysis

Univariate analyses and multivariate logistic regression analyses with backward elimination method were used to evaluate the effects of blood glucose on length of hospitalization (LOH),

**Table 2.** Association Between Length of Hospitalization and Characteristics in a Population of Adults Hospitalized for Acute Exacerbation of Chronic Obstructive Pulmonary Disease

| Category of Hospital Complication | n | Percent of Patients with an In-hospital Complication (n = 24) | Percent of Patients Included in Analysis (n = 209) |
|---|---|---|---|
| Acute renal failure | 3 | (13) | (1) |
| Cardiac | 17 | (71) | (8) |
| Pulmonary | 0 | (0) | (0) |
| Neurologic | 4 | (8) | (2) |
| Health care associated infection | 0 | (0) | (0) |

complications, 30-day hospital readmission, and 90 days all-cause mortality. The other variables considered in multivariate logistic regression models were age, diabetes mellitus (DM) status, sex, steroid use 24 hours before hospitalization, current or past smoker, BMI, inhaled medications at time of presentation, history of chronic steroid use, number of blood glucose measurements taken per day, and respiratory support (invasive and noninvasive ventilation) received during hospitalization.

LOH was considered as a discrete outcome (ie, ≤3 days vs >3 days). In-hospital complication was considered as a categorical variable comparing those patients who had at least 1 complication during the index hospitalization to those who did not, while blood glucose was classified 2 ways: as a discrete variable (at least 1 daily mean <90 mg/dl vs others) and a discrete variable (at least 1 daily mean >140 vs others). All analyses were performed using SAS version 9.2 (SAS Institute Inc., Cary, North Carolina).

## RESULTS

### In-hospital Complications

Twenty-four patients had in-hospital complications (Table 2). Univariate analysis revealed that lower blood glucose (at least 1 daily mean <90 mg/dl vs others) was significantly associated with in-hospital complication by comparing 37.5% of at least 1 daily mean <90 mg/dl at complication group with 9.2% at noncomplication group, $P = 0.0003$, and OR (95% CI = 5.93 (2.26-15.57). Higher blood glucose (at least 1 daily mean >140 mg/dl vs others) was not significantly associated with in-hospital complication by comparing 75.0% of at least 1 daily mean >140 mg/dl at complication group with 82.2% at noncomplication group, $P = 0.40$, and OR (95%CI) = 0.65(0.24-1.77) (Table 3). Multivariate logistic regression analysis with backward elimination method revealed that the lower blood glucose and age at hospital admission were the most significant risk factors for in-hospital complications, where OR (95% CI) = 6.45(2.12-19.66) for the lower blood glucose, and 1.08 (1.01-1.15) for age.

### Length of Hospitalization

Univariate analysis revealed that lower blood glucose was significantly associated with LOH by comparing 20.7% of at least 1 daily mean <90 mg/dl at hospitalization >3 days group with 9.3% at hospitalization ≤3 days group, $P = 0.03$, and OR (95% CI) = 2.55 (1.10-5.92). Higher blood glucose was not significantly associated with LOH by comparing 87.9% of at least 1 daily mean >140 mg/dl at hospitalization >3 days group with 78.8% at hospitalization ≤3 days group, $P = 0.13$, and OR (95%CI) = 1.95(0.81-4.73) (Table 4). Multivariate logistic regression analysis with backward elimination method revealed that respiratory support and in-hospital complication were the most significant risk factors for LOH, where OR (95% CI)) = 4.68 (1.88-11.67) for respiratory support, and 3.74 (1.45-9.67) for in-hospital complication.

### Hospital Readmission Within 30 Days

Thirty-six people were readmitted within 30 days of discharge from index hospitalization. Univariate analysis did not identify any factor associated with 30-day readmission, where OR (95% CI)) = 1.96 (0.75-5.07) and $P$-value = 0.17 for the lower blood glucose, as well as 1.18 (0.45-3.06) and $P$-value = 0.74 for the higher blood glucose. Multivariate logistic regression analysis with backward elimination method failed to reveal any significant risk factor associated with 30-day hospital readmission. (Data not shown.)

### Ninety Day All-cause Mortality

Eight people died due to any cause within 90 days of index hospitalization. Similarly, univariate analysis did not show any factor associated with 90-day all-cause mortality, where OR (95% CI)) = 1.01(0.12-8.52) and $P$-value = 0.996 for the lower blood glucose, as well as 0.36 (0.08-1.59) and $P$-value = 0.18 for the higher blood glucose. Multivariate logistic regression analysis with backward elimination method did not reveal any significant risk factor either associated with 90-day hospital readmission. (Data not shown.)

## DISCUSSION

Our study among hospitalized AECOPD patients on the general medical floor failed to reveal significant relationship between higher blood glucose and adverse clinical outcomes.

Our study differs from the study by Baker et al,[18] which may explain the difference in results. First, our study population was defined based on prior spirometric measurements and World Health Organization (WHO) criteria for exacerbation, whereas the Baker study relied solely on ICD-10 codes. Second, the Baker study did not utilize any radiological data to rule out other pulmonary comorbidities, like pneumonia, which might confer a confounding effect on the data. Third, there were differences in methods for reporting blood glucose data. Studies utilized either a single admission blood glucose,[8-11] daily mean blood glucose,[14,15] or a single blood glucose obtained (fasting or nonfasting) during

**Table 3.** Association Between In-hospital Complications and Characteristics in a Population of Adults Hospitalized for Acute Exacerbation of Chronic Obstructive Pulmonary Disease

| | Complications During Index Hospitalization | No. Complications During Index Hospitalization | Univariate Analysis | | |
|---|---|---|---|---|---|
| **Characteristic** | **n = 24** | **n = 185** | **OR** | **95% CI** | ***P*-value** |
| Blood glucose: at least 1 daily mean >140mg/dl – n (%) | 18 (75.0) | 152 (82.2) | 0.65 | 0.24-1.77 | 0.40 |
| Blood glucose: at least 1 daily mean <90mg/dl – n (%) | (37.5) | 17 (9.2) | 5.93 | 2.26-15.57 | 0.0003 |
| Age (years) at hospital admission – mean (sd) | 67.3 (9.5) | 64.5 (8.1) | 1.05 | 0.99-1.11 | 0.11 |
| Diabetes Mellitus at hospital admission – n (%) | 7 (29) | 56 (30) | 0.95 | 0..37-2.42 | 0.91 |
| Male sex – n (%) | 7 (29) | 73 (39) | 0.63 | 0.25-1.60 | 0.33 |
| Corticosteroids given within 24 hours of hospitalization – n (%) | 24 (100) | 176 (96) | * | | |
| Current smoker – n (%) | 8 (33) | 75 (41) | 0.73 | 0.30-1.80 | 0.50 |
| Body mass index in kg/m$^2$ – mean (sd) | 32.6 (8.7) | 31.1 (8.8) | 1.02 | 0.97-1.07 | 0.45 |
| Inhaled medications at the time of presentation – n (%) | 20 (83) | 165 (89) | 0.61 | 0.19-1.95 | 0.40 |
| History of chronic steroid use – n (%) | 1 (4) | 21 (11) | 0.34 | 0.04-2.63 | 0.30 |
| Received respiratory support during hospitalization – n (%) | 5 (21) | 23 (12) | 0.54 | 0.18-1.59 | 0.26 |
| Number of blood glucose measurements taken per day –mean (sd) | 1.7 (1.9) | 2.6 (1.8) | 0.66 | 0.47-0.93 | 0.02 |

**Table 4.** Association Between Length of Hospitalization and Characteristics in a Population of Adults Hospitalized for Acute Exacerbation of Chronic Obstructive Pulmonary Disease

| | Hospitalization > 3 Days | Hospitalization ≤ 3 Days | Univariate Analysis | | |
|---|---|---|---|---|---|
| **Characteristic** | **n = 58** | **n= 151** | **OR** | **95% CI** | ***P*-value** |
| Blood glucose: at least 1 daily mean>140mg/dl – n (%) | 51 (87.9) | 119 (78.8) | 1.95 | 0.81-4.73 | 0.13 |
| Blood glucose: at least 1 daily mean<90mg/dl – n (%) | 12 (20.7) | 14 (9.3) | 2.55 | 1.10-5.92 | 0.03 |
| Age (years) at hospital admission – mean (sd) | 64.6 (8.5) | 64.9 (8.3) | 0.996 | 0.96-1.03 | 0.85 |
| Diabetes Mellitus at hospital admission – n (%) | 21 (36.2) | 42 (27.8) | 1.47 | 0.77-2.80 | 0.24 |
| Received respiratory support during hospitalization – n (%) | 17 (29.3) | 11 (7.3) | 5.28 | 2.29-12.16 | <0.0001 |
| Complications during hospitalization – n (%) | 14 (24.1) | 10 (6.6) | 4.49 | 1.86-10.81 | 0.0004 |
| Male sex – n (%) | 21 (36.2) | 59 (39.1) | 0.89 | 0.47-1.66 | 0.70 |
| Corticosteroids given within 24 hours of hospitalization – n (%) | 56 (96.6) | 144 (96.0) | 1.17 | 0.23-5.95 | 1.000 |
| Current smoker – n (%) | 21 (36.2) | 62 (41.1) | 0.82 | 0.44-1.52 | 0.52 |
| Body mass index in kg/m$^2$ – mean (sd) | 32.4 (9.9) | 30.9 (8.4) | 1.02 | 0.98-1.06 | 0.29 |
| Inhaled medications at the time of presentation – n (%) | 55 (94.8) | 130 (86.1) | 2.96 | 0.85-10.34 | 0.08 |
| History of chronic steroid use – n (%) | 8 (13.8) | 14 (9.3) | 1.55 | 0.62-3.93 | 0.35 |
| Number of blood glucose measurements taken per day – mean (sd) | 2.6 (2.5) | 2.9 (2.0) | 0.94 | 0.81-1.09 | 0.43 |

hospitalization.[10,18,19,21-23] Our study utilized a daily mean blood glucose, since blood glucose levels among AECOPD patients on systemic corticosteroids tend to peak around afternoon and evening hours.[29] Therefore, blood glucose measurements taken throughout the day more accurately capture patients' glycemic status, although all of the approaches discussed are imperfect.

Our a priori expectation that adverse outcomes in hospitalized AECOPD patients would be associated with the higher blood glucose (as noted in recent observational data) was not validated. In fact, our study revealed that the lower blood glucose levels resulted in higher risk for in-hospital complication, and in-hospital complication resulted in longer duration of hospitalization. Therefore, lower blood glucose may indirectly result in longer duration of hospitalization. The occurrence of normal or lower blood glucose among AECOPD patients is not common, since COPD exacerbation is characterized by an inflammatory process involving prohyperglycemia agents like stress hormones and cytokines,[30-32] and patients routinely are treated with systemic corticosteroids that increase blood glucose.

Recent data show that the lower blood glucose is associated with adverse outcomes in other conditions including increased morbidity and mortality.[10,33-38] The presence of hypoglycemia itself may be a marker for severity of illness, may have direct consequences itself, or be a treatment related side-effect. The presence of hypoglycemia, independent of treatment-related effects, may reflect defects in glucose counter-regulation, an imbalance between reduction in circulating insulin and enhanced glucagon secretion in response to lower glucose levels, or aberrant physiologic response to falling glucose levels. Therefore, the patient's inability to mount a hyperglycemic response in the presence of these 2 biochemical processes might portend an adverse clinical outcome. Our study is the first to demonstrate that hypoglycemia as defined by a blood sugar less than 90 mg/dl in patients with AECOPD is associated with adverse clinical outcomes.

This study was performed in a rural, white population, which limits its generalizability to other populations. The role of ste-

roids in the treatment of COPD exacerbations has long been established,[21,22,32,39] but we were unable to collect data regarding corticosteroid dosage, which is highly variable in clinical practice. Corticosteroid dosage likely exerts great influence on blood glucose trends, but the clinical importance of these fluctuations remains unclear. Although we looked at patients with spirometry, baseline disease severity per WHO/GOLD criteria staging was not included in our analysis. Also, it is important to note that although our study is large compared to previous studies, it is possible that it was not large enough to have the power necessary to detect the significant relationship between higher blood sugars and adverse outcomes in this population. Therefore, further larger studies in this population to incorporate this data would help to elucidate the complex interactions between metabolic control of blood glucose, extraneous hyperglycemic agents, and clinical outcomes.

## CONCLUSION

Our study differed from previous studies by the absence of a relationship between adverse outcomes and increased blood glucose levels. Interestingly, we found that blood sugars less than 90 mg/dl were associated with in-hospital complication and may indirectly result in longer LOH. Further studies examining dose and duration of steroid dose, as well as stratification based on spirometric data, may provide further insights of the many subtleties and complexities of this association on LOH and adverse medical complications.

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CME

To receive CME credit, complete this quiz and return it to the address listed below. See CME-designated article on pages 244-249.

# Quiz: Association Between Blood Glucose Level and Outcomes in Patients Hospitalized for Acute Exacerbation of Chronic Obstructive Pulmonary Disease

## EDUCATIONAL OBJECTIVES

Upon completion of this activity, participants will be able to:

1. Appreciate the factors associated with adverse clinical outcomes in patients hospitalized with an acute exacerbation of chronic obstructive pulmonary disease (AECOPD).
2. Recognize the role that an altered blood glucose level may have on hospitalized patients with AECOPD and other acute illnesses.

**PUBLICATION DATE:** December 16, 2013

**EXPIRATION DATE:** December 16, 2014

## QUESTIONS

1. Chronic obstructive pulmonary disease is a chronic condition affecting 50 million people and is the sixth leading cause of death in the United States, with in-hospital mortality ranging from 2% to 30%.
   - ❑ True
   - ❑ False
2. Adverse outcomes of AECOPD are associated with:
   - ❑ Lower arterial pH, older age, female gender
   - ❑ Underlying comorbidities, disease severity, in-hospital complications
   - ❑ In-hospital complications, lower arterial pH, younger age, male gender
   - ❑ Underlying comorbidities, disease severity, in-hospital complications, higher arterial pH, older age, male gender
   - ❑ None of the above
3. Data from other studies have shown that higher blood glucose is associated with adverse outcomes among patients with acute myocardial infarction, brain injury, community-acquired pneumonia, severe trauma, critical illness, and those undergoing cardiothoracic surgery.
   - ❑ True
   - ❑ False
4. Hospitalized COPD patients with elevated blood glucose have been found in other studies to have longer hospital stays, more frequent isolation of gram negative bacteria, ventilatory failure, and a higher mortality risk.
   - ❑ True
   - ❑ False
5. The present study revealed a significant relationship between higher blood glucose levels and adverse clinical outcomes among patients hospitalized with AECOPD.
   - ❑ True
   - ❑ False
6. The present study revealed that among patients hospitalized with AECOPD, a lower blood glucose level was a significant risk factor associated with an in-hospital complication and increased hospital length of stay.
   - ❑ True
   - ❑ False
7. In the present study of patients with AECOPD, hospital readmission within 30 days and 90-day all cause mortality were significantly increased in patients with both increased and decreased blood sugar levels during hospitalization.
   - ❑ True
   - ❑ False

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You may earn CME credit by reading the designated article in this issue and successfully completing the quiz (75% correct). Return completed quiz to *WMJ* CME, 330 E Lakeside St, Madison, WI 53715 or fax to 608.442.3802. You must include your name, address, telephone number, and e-mail address.

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# Associations Between Social Media Displays and Event-specific Alcohol Consumption by College Students

Megan A. Moreno, MD, MSEd, MPH; Lauren Kacvinsky, BS; Megan Pumper, BA; Leah Wachowski, Jennifer M. Whitehill, PhD

## ABSTRACT

**Background:** The Mifflin Street Block Party is a yearly Wisconsin event known for high levels of alcohol consumption and previous negative outcomes. This study investigated displayed Mifflin references on Facebook and their association with alcohol consumption at the block party.

**Methods:** Participants included first-year college students who were enrolled in a longitudinal study involving Facebook profile assessments and interviews. We identified a subset of participants who were interviewed within 28 days following the Mifflin St Block Party. Participants were categorized as "Mifflin Displayers" or "Non-displayers" based on Facebook profile content. Interviews included the timeline follow-back method to assess alcohol use in the past 28 days. Analysis included logistic and linear regression.

**Results:** Among the 66 participants included in this study, 45 (68.2%) were female and 38 (50%) were Mifflin Displayers on Facebook. Among the Mifflin Displayer participants, 18 (27.2%) displayed prior to Mifflin, 11 displayed the day of Mifflin (16.7%) and 19 (28.8%) displayed after. Some participants displayed in more than 1 time frame. A total of 40 (60.6%) reported alcohol use on the day of the Mifflin Street Block Party. The mean number of drinks reported on the day of Mifflin was 8.8 (SD = 6.1), with a range of 1 to 35. Displayed references to Mifflin on Facebook were positively associated with reporting alcohol use at Mifflin (OR = 20.9, 95% CI 5.6-78.8).

**Conclusion:** Displaying Facebook references to Mifflin was associated with alcohol consumption on the day of the event. Future prevention efforts could consider creating Facebook advertisements with safety messages triggered by Mifflin displays.

## INTRODUCTION

Alcohol use, although common, is a major cause of both morbidity and mortality among college students in the United States.[1] Approximately half of students who use alcohol report direct alcohol-related harms, and as many as 1700 college student deaths each year are alcohol-related.[2,3]

While rates of daily drinking are low in this population, many college students report drinking heavily on particular occasions such as weekends or holidays.[4] Previous work has examined large alcohol-themed events and parties such as New Year's Eve, St Patrick's Day, spring break or Halloween.[5] These events have been associated with heavy alcohol use, even among students who do not ordinarily drink.[6,7] Previous work has illustrated associations between heavy alcohol at these events and negative health and behavioral consequences, including drinking and driving, and committing acts of theft or vandalism.[8] The risk of attending such events may be particularly salient among the first-year college student population. Approximately 20% of students who did not drink heavily in high school initiate this behavior upon arrival at college. Initiation at a large-scale event may present additional risks, given these students' lack of experience with drinking.[9] For other first-year students, arrival at college is associated with a move from experimentation to frequent alcohol use that may be influenced by large alcohol-themed events.[10]

One event with significance to alcohol use on the University of Wisconsin-Madison campus is the Mifflin Street Block Party (Mifflin). This party is an annual celebration held on Mifflin Street on the first Saturday of May that includes widespread consumption of alcoholic beverages. In 2011, the Mifflin Street Block Party had a larger and more intoxicated crowd. This was the first year that open containers were allowed on sidewalks and front yards if the attendee had a wristband. Police reports from the 2011 Mifflin party showed increased crime and violence, including stabbings, sexual assaults, thefts ,and drug dealing. In total, the Madison Police Department arrested 162 people on 204 tentative charges.[11] In 2012, no drinking was allowed on sidewalks or the street, and crowds were back to the normal level of approximately 5000. However, the number of arrests was higher,

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likely related to arrests for open containers and underage consumption.[12] While many feel that control over Mifflin improved after the negative outcomes from 2011, this event remains a time of high alcohol consumption and risks for negative health, legal, and social outcomes.

These alcohol-themed events present unique challenges for both universities and parents in providing appropriate guidance and promoting safety. Universities face challenges in anticipating attendance rates and sending appropriate prevention messages to students prior to the event, as well as ensuring safety during the event. Parents face challenges in understanding these events and providing guidance appropriate to their college students' life stage. New approaches for understanding these alcohol-themed events and providing event-specific anticipatory guidance to potential attendees are needed.

One novel approach to consider when investigating alcohol-themed events among college students may be social networking sites such as Facebook. These websites are popular among and consistently used by college students; up to 98% of college students use Facebook.[13,14] References to alcohol use are common on social networking sites; up to 83% of college students' profiles reference alcohol.[15] Our previous work investigated college students' displayed references to alcohol use and problem drinking.[16] We found that college students who referenced intoxication or problem drinking on their Facebook profiles were more likely to score as at risk for problem drinking using the Alcohol Use Disorders Identification Test (AUDIT).[17] It is unclear how students use social media to display their attitudes, intentions, or behaviors regarding alcohol-themed events. It is possible that Facebook may provide novel opportunities to identify students planning to attend such events towards providing anticipatory guidance.

The purpose of this study was to investigate references to the Mifflin Street Block Party on Facebook. For this study we chose to focus on first-year students, who are at high risk if attending this event, given that they are underage and generally have less experience with alcohol use compared to their upperclassmen peers. Our goals were to describe displayed references to Mifflin on Facebook and understand associations between this displayed content and alcohol behaviors on the day of the Mifflin event.

## METHODS

Data were collected between April 16, 2012 and June 2, 2012. This study received approval from the Institutional Review Board of the University of Wisconsin–Madison.

### Setting and Participants

Participants were selected from an ongoing study of 199 first-year college students at the University of Wisconsin-Madison that involved yearly interviews and monthly Facebook profile evaluations for displayed references to alcohol. The participants in the ongoing study were randomly selected from the registrar list of incoming first-year students and were recruited the summer prior to enrolling in college. Potential participants received a pre-announcement postcard and then were contacted through e-mail, phone calls, and Facebook messages over a period of 3 weeks. Eligibility was based on being 18 or 19 years old and being enrolled as first-year, full-time students for fall 2011. The response rate was 52.8%.

From this larger study population, we identified a subset of participants for the present study. Inclusion criteria for this study included completing a phone interview within 28 days of Mifflin so that quantity and frequency of alcohol use on the day of Mifflin could be assessed using the validated timeline follow-back procedure described below.[18] We then reviewed the Facebook coding data and interview data collected during that time period for this subset of participants.

### Consent Process and Facebook Friending

During the consent process for the ongoing study, potential participants were informed that this was a longitudinal study involving intermittent phone interviews as well as evaluation of Facebook profiles, and that linking to our research team profile via "friending" was a requirement of the study. Participants were informed that Facebook content would be viewed, but that no one on the research team would post any information to the participant's profile. Participants were asked to maintain open security settings with our research team.

### Coding Procedure

The Facebook profile of each participant was evaluated during the time period including 1 month prior to and 1 month after Mifflin. During this profile evaluation, a trained coder recorded displayed references to alcohol as well as to Mifflin using a codebook specific to evaluating social media alcohol displays.[19] Data included the coder's typewritten description of any image references (ie, photographs or graphics) or verbatim text from participant profiles (ie, status updates, wall posts, likes/groups, or comments). Identifying information, if present, was removed from text references. Sections of the Facebook profile that were evaluated included the wall, photographs, likes/groups, and events.

### Codebook and Variables

For the purposes of this study, we evaluated displayed Facebook references to the Mifflin Street Block Party. Image references included photos of participants attending th party or wearing shirts or other apparel that referenced Mifflin. Text references included any status updates, wall posts, or comments that referenced Mifflin. An example of a text reference to Mifflin would be a status update saying, "Only three more days till Mifflin!" References to Mifflin also included "liking" the Mifflin Street

Block Party Facebook page. Facebook users also have the option of using an "events" function to indicate their attendance at a particular event. When participants used this Facebook function to indicate that they were attending the Mifflin Street Block Party event, it was recorded as a Mifflin reference. Details for the first 3 displayed references by each Mifflin Displayer participant included the format of these references (eg, status update, photograph, like/group or event).

### Interview Procedure

The ongoing study included 2 types of interviews: yearly phone interviews conducted with all participants near the end of each academic year, and prompted phone interviews conducted if the participant displayed alcohol references on the profile. Interviews were scheduled at the participants' convenience. The present study included participants who had a yearly or prompted interview within 28 days of the Mifflin event. Interviews lasted between 40 and 60 minutes on average, data collection during interviews was done with a spreadsheet and written notes were taken for qualitative questions. Participants were provided $35 for completion of their interviews.

### Interview Variables

Interviews assessed alcohol behaviors including current use (past 28 days). For participants who reported current use of alcohol, we used the timeline follow-back (TLFB) method to assess quantity and frequency of alcohol use.[18] During this validated procedure, the interviewer works with the participant to review each day of the past 28 days to assess how many standard alcohol drinks were consumed. Standard alcohol drinks were defined as per National Institute of Alcohol Abuse and Alcoholism guidelines, which includes a 12-ounce serving of beer.[20] This procedure leads to the following measured outcomes: total number of alcoholic drinks, total number of drinking episodes and total calculated number of binge drinking episodes in the past 28 days. This procedure also allows identification of whether alcohol use took place on a particular day, such as the day of the Mifflin Street Block Party.

### Analysis

Descriptive statistics were calculated for displayed references to Mifflin on Facebook. To calculate number of drinks on Mifflin, TLFB data for each participant on the date of the Mifflin party was used. We used logistic regression to determine associations between Mifflin displays on Facebook and self-reported alcohol use on Mifflin via the TLFB. We used linear regression to determine associations between number of displayed Mifflin references on Facebook and number of reported drinks at Mifflin. Both models were adjusted for gender and analyses stratified by gender were also conducted. All *P* values were 2-sided, and $P < .05$ was used to indicate statistical significance. Statistical analyses were performed using Stata version 10 (StataCorp LP, College Station, Texas).

**Table 1.** Demographic Information for Participants

| N=66 | N (%) |
|---|---|
| **Gender** | |
| Female | 45 (68.2%) |
| Male | 21 (31.8%) |
| **Ethnicity** | |
| White | 63 (96%) |
| Non-white | 3 (4%) |

## RESULTS

A total of 66 participants were identified and included in this study, among whom 45 (68.2%) were female and 96% were white (Table 1). The sample included participants who had a yearly (N=39) or prompted interview (N=27) within 28 days of the Mifflin event. Of the prompted interviews, 13 interviews were prompted by displayed references to Mifflin, 14 were prompted by other non-Mifflin displayed references to alcohol use. Reviewing Facebook coding data for this sample, 38 (50%) had displayed about Mifflin on Facebook by 28 days after the event.

### Displayed Mifflin References on Facebook

Among the participants who displayed references to Mifflin on Facebook, 18 (27.2%) displayed prior to Mifflin, 11 displayed the day of Mifflin (16.7%), and 19 (28.8%) displayed after the event. Some participants displayed in more than 1 time frame.

The mean number of displays was 4.5 (SD 7.4), with a median of 1, range of 1 to 37. References were displayed on Facebook in all areas of the profile, including status updates, pictures, likes/groups and events (Table 2).

### Alcohol Behaviors at the Mifflin Street Block Party

Among the 66 participants, 51 (77.2%) reported alcohol use in the past 28 days at the time of their interview. A total of 40 (60.6%) reported alcohol use on the day of Mifflin. The mean number of drinks reported on the day of Mifflin was 8.8 (SD=6.1), with a range of 1 to 35. Among women, the mean number of drinks was 7.4 (SD 4.4) with a range of 1 to 20. Among men the mean was 12.3 (SD 8) with a range of 6 to 35.

### Associations Between Mifflin Facebook Display and Alcohol Behavior at Mifflin

Displayed references to Mifflin on Facebook were positively associated with reporting alcohol use at Mifflin (OR=20.9, 95% CI 5.6–78.8). When examining these results stratified by gender, relationship was significant for both women (OR=32, 95% CI: 5.6–183.1) and men (OR=10.5, 95% CI: 1.3–81.1).

The number of displayed references to Mifflin on Facebook also was positively associated with the number of drinks reported at Mifflin (*B*=5.4; 95% CI: 0.4–10.4). Examining this relationship by gender illustrated that for females, the relationship

**Table 2.** Examples of Displayed Mifflin References on Facebook and Estimated Prevalence (Time Period = 1 Month Prior Through 1 Month After the Mifflin Street Block Party)

| Examples of Mifflin References | Estimated proportion of displayed Mifflin references |
|---|---|
| **Status Updates** | 20.8% |
| "Let Mifflin begin" | |
| "Here we go...MIFFLIN!!" | |
| **Photos** | 66.7% |
|  | |
|  | |
| **Likes/Groups** | 10.4% |
|   | |
| **Event**[a] | 2.1% |
|  | |

[a] Regarding the Mifflin event function on Facebook: For this study we included only displayed Facebook references to Mifflin in the time period of 1 month prior to 1 month after Mifflin; however, many participants joined this event on Facebook months prior to that time period. This number is likely a very conservative estimate, also illustrated by the 12,478 other guests who joined this event noted in the screen shot.

remained significant ($B$=5.5, 95% CI: 0.28=10.8). For males, this relationship was not significant ($B$=5.2, 95% CI: -6.7–17.1).

## CONCLUSION

Findings from this study suggest that among our sample of first-year college students, references to Mifflin were displayed on Facebook in a variety of different multimedia formats including text, images, and planning tools. Participants displayed Mifflin references before, on the day of, and following the event. These references were associated with a high likelihood of drinking on the day of the event, and increased references were associated with higher number of drinks reported.

Many participants displayed references to Mifflin in the month prior to the event. These references included responding to a Facebook event invitation and displaying text suggesting excitement about or anticipation of the event. A high prevalence of displayed Mifflin content prior to the event warrants concern and represents potential opportunity. One concern regarding Mifflin displays on Facebook pre-event is that these messages could raise awareness of this event and encourage other students to attend. Peers are well understood to be a source of influence among adolescents, including older adolescent college students.[21] At their most extreme, these peer displays could result in peer pressure to attend.

Mifflin references that were displayed prior to the event also represent an area of opportunity. It is possible that these references could be linked to prevention messages via Facebook advertisements. Advertisements on Facebook are triggered by keywords displayed on the profile. For example, displayed text references to terms such as "diet" will trigger advertisements for weight loss services displayed next to the profile. It is possible that universities could choose to place safety or prevention messages targeted to keywords such as "Mifflin" in the month leading up to this event. This approach would be limited in that it would only work for displayed text related to Mifflin, and would not provide linked messages tied to photographs, which made up many Mifflin references in this study. However, it may provide a way to deliver targeted, inexpensive messages in a setting in which college students are discussing and making plans for Mifflin.

Before such efforts can move forward, a better understanding of what type of messages would be acceptable to the college population as "pop up" advertisements should be undertaken. In 2012, social media was used as a venue in which to spread messages directing students to avoid Mifflin. The "don't go" YouTube video created by Dean of Students Lori Berquam spread virally after it was altered into humorous versions set to music. While 1 video had over 80,000 views,[22] it is unclear whether these well-intentioned efforts were successful in deterring students from attendance at Mifflin.

Study findings illustrated that among female college students, an increasing number of references to Mifflin were positively associated with the number of drinks reported on the day of Mifflin. This relationship was not significant among males. This may be related to gender differences in how, and how often, Facebook is accessed by females compared to males. Previous work has illustrated that women are more frequent social networking site users compared to men.[23] It is possible that if advertisements were created to disseminate prevention messages to students triggered by Mifflin displayed content, these should be targeted by gender.

Much is understood about the different motivations and expectancies that males and females have towards alcohol, so it is likely that this previous work could guide the creation of a gender-specific message.[7]

It also is important to note that the study participants represent first-year college students, all of whom were underage at the time of Mifflin. Approximately 60% of interviewed students reported alcohol use on the day of Mifflin. The heavy alcohol consumption reported by this group at this event is thus worrisome; the mean number of drinks reported was 9, which is well above standard definitions for a binge drinking event.[24] It is unclear what motivates underage first-year students to attend this party. It is possible that after almost a year of experience at the University that some students have accepted the common social norm of the University of Wisconsin-Madison as a "party school." UW–Madison has repeatedly been listed in the top "party colleges" in the United States.[25] This reputation, along with the reinforcement of this reputation through displayed alcohol references on Facebook such as the ones found in this study, could lead some first-year students to accept alcohol use as a normative and part of the college experience. Regardless of the motivations to attend, our study findings suggest that the event was attended by first-year college students, among whom drinking rates were high and the frequency of displayed references to Mifflin on Facebook were common.

Limitations to our study include a small sample size drawn from a larger study not explicitly designed to evaluate Facebook displays related to the Mifflin event. Though the participants in the larger study represent a random sample of undergraduates from UW–Madison, this study included participants who had an interview within 28 days of the Mifflin event, which was not a random sample. However, the participants' involvement in an ongoing study that included Facebook profile evaluation in the time period surrounding the Mifflin event, as well as use of a validated quantity/frequency measure (TLFB) to assess alcohol use on the day of Mifflin provided a unique opportunity to use existing data to address an event of important local concern. Another limitation is that while we used the TLFB to achieve a validated measure of the number of drinks consumed on the day of Mifflin, we did not clarify with participants that their drinking took place at that event. Yet, given the numerous photographs displayed on Facebook at Mifflin it seems likely that many if not most of the participants who reported alcohol use on that day were in attendance at this event.

Despite these limitations, our small study suggests important implications. Facebook may present new opportunities for universities such as UW–Madison to create prevention messages and target them to students displaying this content. These advertisements could be targeted at students. It also is possible that these study findings could be used to create educational messages directed at parents of first-year students. Parents increasingly use Facebook, and many are likely "friends" with their college student child.[26] This group may be interested partners in reinforcing prevention messages if references to Mifflin are noted on their child's profile.

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# Development of a Pilot Family Medicine Hand-carried Ultrasound Course

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## ABSTRACT

**Background and Objectives:** A hand-carried ultrasound training session was organized as an initial step in developing a long-term ultrasound education program for family medicine residents and faculty. Comparative effectiveness studies examining the potential benefits, risks, and any possible cost savings associated with this technology will be predicated on having a sufficient number of primary care physicians trained and able to use hand-carried ultrasounds as part of routine care. The proposed training described here is a first step toward this broader conversation and empirical study of hand-carried ultrasound use in family medicine.

**Methods:** An 8-hour training consisting of didactic lectures, case review, and hands-on experience imaging standardized patients with ultrasound machines and an ultrasound simulator. The objective of the course was to introduce focused ultrasound acquisition and interpretation of the gall bladder, kidney, heart, and abdominal aorta to family medicine physicians. Participating physicians were evaluated for changes in self-perceived comfort and proficiency with the hand-carried ultrasound before and after the training.

**Results:** Statistically significant changes for most comfort and proficiency items were demonstrated. Importantly, the only item that did not show significant change dealt with basing clinical decisions on information obtained from the device.

**Conclusion:** The subjective improvement suggests this approach is one potentially useful hand-carried ultrasound training framework. Future work should attempt to further develop curricula and address issues such as longitudinal training assessments and certification and the development of competency in the necessary skill sets.


## INTRODUCTION

Innovation in ultrasound technology has led to the development of the hand-carried ultrasound.[1] With their small size and increased mobility, hand-carried ultrasounds allow for the possibility for all physicians to carry ultrasounds for use in patient care, regardless of the care setting. In conjunction with a history and physical, the use of a hand-carried ultrasound has implications in screening and diagnosing certain pathology[2,3] through point-of-care ultrasonography. Point-of-care ultrasound is defined as ultrasonography that can be brought to the patient and performed by the provider in real time.[4] Point-of-care ultrasonography done with hand-carried machines has been shown to be effective in supplementing the cardiovascular examination in selected patient populations[5] while identifying cardiovascular and abdominal pathology[6-11] with comparable accuracy to stand-alone ultrasound units.[12,13,14] It also has demonstrated that it has a role in inpatient internal medicine, emergency medicine, and obstetrics/gynecology.[11,12]

The concept of using point-of-care ultrasonography with hand-carried ultrasounds in a family medicine setting is a relatively novel idea that, from our literature review, has yet to be substantially explored. The success that hand-carried ultrasound has had on patient care in other medical specialties inspired our family medicine department to begin to investigate potential applications in our residency training programs. We began to consider how point-of-care ultrasonography with hand-carried ultrasounds may be used in a family medicine setting. For example, one scenario might involve a 65-year-old male with a smoking history and a palpable abdominal mass. The US Preventative Task Force provides a Grade B recommendation of abdominal aortic aneurysm screening in male patients 65 to 75 years of age with a smoking history.[15] Instead of having the patient wait to schedule an appointment with radiology and risk being lost to follow-up, the ultrasound examination can be done instantaneously and managed much earlier.

Another possible scenario would be one in which a teenager is undergoing a sports physical. A quick cardiac scan with a hand-

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**Table 1.** Review of Focused Ultrasound Training Courses

| Author | Title of Paper | Trainee | Training Lecture | Practice | Results |
|---|---|---|---|---|---|
| Alexander et al[19] | Training and accuracy of non-cardiologists in simple use of point-of-care echo: A preliminary report from the Duke Limited Echo Assessment Project | 16 internal medicine residents and 4 beginning cardiology fellows | 3 hour HCU training program consisting of 30 minutes of introduction to ultrasound and the HCU device, 75 minutes of case review, 75 minutes of hands-on practice | 75 minutes of hands-on practice | Average time to complete HCU echo was 8.5 minutes and was able to improve assessment of LV function and pericardial effusion |
| Croft et al[20] | The echo stethoscope: Is it ready for prime time by medical students? | Medical students | 30 hours of didactic lecture and observation of echo exams | 40 supervised practice echocardiograms | Students were able to use ultrasound to be diagnostic in >90% of the patients, interpreted correctly in >80% of patients |
| Croft et al[21] | Impact of front-line, limited, focused, and expedited echocardiography in the adult emergency department using a compact echo machine | Medical student and echo cardiologist | | | Changed diagnosis in >25% of patients and management in >15% of patients |
| DeCara et al[17] | The use of small personal ultrasound devices by internists without formal training in echocardiography | 3 internal medicine residents | 20 hours of didactic lecture | 20 supervised practice echocardiograms | Residents and echocardiographers had similar sensitivity and specificity, but echocardiographers had higher PPV and sensitivity |
| Kimura et al[5] | Usefulness of a hand held ultrasound device for bedside examination of left ventricular function | 13 internal medicine residents | 1 hour of review lecture, 1 hour of videotaped examples of normal and abnormal systolic function | 5 practice echocardiograms on normal volunteers | 10 residents showed improvement in accuracy, 2 residents no net improvement, 1 resident worsened in diagnostic accuracy |
| Rugolotto et al[22] | The new generation of hand-carried echocardiographs: the Stanford view | Internal medicine residents | 10 hour training curriculum | | Residents used HCUs to decrease discrepancies from physical exam from 33.2% to 27.8% |

Abbreviations = HCU, hand-carried ultrasound ; LV, left ventricular.

carried ultrasound might reveal hypertrophic cardiomyopathy and prevent a sudden cardiac arrest. These are both hypothetical scenarios in which point-of-care ultrasonography with hand-carried ultrasounds may have a positive impact on patient care. However, since there is little literature on the impact of point-of-care ultrasonography on clinical decision-making and patient care cost/benefit in the family medicine setting, more research is needed. Before this research can be conducted broadly, family medicine physicians must learn how to use hand-carried ultrasounds.

In addressing ultrasound training, studies have shown that it is possible to train residents and medical students using 5 to 20 hours of focused ultrasound training courses to perform various narrowly defined tasks.[5,11,13,14,16-18] These findings are summarized in Table 1. While there are lengthy medical school ultrasound curriculums designed to teach medical students how to use ultrasound,[23] these curriculums may not be the best choice for busy family medicine residents and faculty due to time and budget constraints.

The current effort describes an evaluation of a pilot short course for hand-carried ultrasound training specifically designed for and implemented within the family medicine context. It emphasized brief, focused training strategies, and assisted us in identifying participants with a strong interest in adopting hand-carried ultrasound point-of-care ultrasonography in our residency programs. The study attempted to identify positive and negative aspects of the various components of the hand-carried ultrasound training session, explored areas of need for future training, and assessed impact on participants' self-perceived comfort and proficiency performing hand-carried ultrasound tasks.

## METHODS

A hand-carried ultrasound training session was organized for 8 faculty members from the Medical College of Wisconsin's Department of Family and Community Medicine who volunteered to participate. The study was granted exempt status by the institutional review board.

The majority of the participants had 0 to 10 hours of ultrasound experience, with 1 participant having over 40 hours and completion of a prenatal ultrasound course. An emergency department physician who completed an emergency medicine ultrasound fellowship, with American Registry for Diagnostic

Medical Sonography certification and 20 years of point-of-care ultrasonography experience, led a training session consisting of lectures, case review, and hands-on experience imaging 4 standardized patients with normal anatomy using Vscan and LOGIQ E ultrasound machines (GE Healthcare, Waukesha, Wisconsin) and an Ultrasim ultrasound simulator (Med Sim Inc., Fort Lauderdale, Florida) which demonstrated commonly encountered sonographic pathology. The Vscan is a hand-carried ultrasound, while the LOGIQ E is a stand-alone ultrasound machine. The larger LOGIQ E was used to provide the participants with the ability to see images on a larger display in higher resolution. The LOGIQ E allowed the participants to orient themselves to the images first and then transfer their understanding of what the images look like to the smaller interface of the Vscan. The areas of clinical focus included identification of normal anatomy and pathologic findings of the abdominal aorta, heart, liver, gall bladder, and kidney. These anatomical areas of focus were chosen based on the assumption that they would be most relevant for a family medicine setting. The amount of time spent on each topic is found in Table 2.

**Table 2.** Topics and Time Spent

| Topic | Time Spent (minutes) |
|---|---|
| Machine use and knobology | 15 |
| Ultrasound physics and areas of clinical focus | 15 |
| Abdominal aorta and gall bladder review of exam techniques | 45 |
| Hands on with standardized patients and ultrasound simulator | 120 |
| Abdominal aorta and gall bladder | |
| Case reviews | 30 |
| Cardiac review of exam technique | 60 |
| Hands on with standardized patients - cardiac | 60 |
| Evaluation of participants | 30 |

**Table 3.** Frequency of Participants Ordering and Performing Certain Ultrasound Exams

| Type of Ultrasound Exam | Modal Responses of Participants' Rate of Ordering Exam | Modal responses of Participants' Rate of Performing Exam |
|---|---|---|
| Aorta | Rarely | Never |
| Kidney | Sometimes | Never |
| Liver | Frequently | Never |
| Cardiac | Frequently | Never |

Participants completed a pretraining and posttraining survey to gauge change in their self-perceived confidence and proficiency in performing a hand-carried ultrasound exam. A questionnaire with a 7-point Likert-type scale was developed with each item ranging from 1 (strongly disagree) to 7 (strongly agree) and additional open-ended responses. The open-ended responses allowed for participants to provide input and thoughts about various topics such as how hand-carried ultrasound would be used in a family medicine setting. The scaled items are summarized in Table 4. The instrument was not validated, but may serve as a starting point for hand-carried ultrasound-specific perception and performance assessment. The pretraining and posttraining surveys and evaluations were anonymous and number coded to allow for linkage of the instruments.

## RESULTS

Participants assessed their level of confidence and self-perceived proficiency with hand-carried ultrasounds before and after training. The Wilcoxon Signed Rank Sum test was used to compensate for non-normality due to the small sample size and near uniform unfamiliarity with hand-carried ultrasounds among the participants (Table 4).

Significant improvement was found for all items post-test except for 1 item on participants' comfort basing clinical decisions on point-of-care ultrasounds they performed. Following the training, all the participants appeared to be able to locate all sonographic anatomy as judged by the course evaluators. However, this evaluation was performed in an observational manner using a checklist and was not standardized due to time constraints.

Participants rated their level of frequency of ordering and performing of different ultrasound exams using the responses "never," "rarely," "sometimes," and "frequently," scaled from 1 to 4 (Table 3).

In response to the open-ended training evaluation questions, the participants stated that the hands-on experience with standardized patients was the most effective education, followed by the review and discussion of case studies and the use of the ultrasound simulator. All participants believed it was important to learn how to use ultrasound for both patient care and resident education. Prior to the training, participants rated the importance of performing abdominal (85% agreement) and cardiac ultrasounds (50% agreement). No change in agreement was observed after the training. The higher level of importance in performing the abdominal exam may be due to participants treating more patients with abdominal issues than those with cardiac issues. All participants stated they would be willing to use a hand-carried ultrasound in clinic.

## DISCUSSION

In this sample of family physicians, a statistically significant change in several important components required for successful ultrasound utilization was noted. These include comfort and confidence in selecting the appropriate ultrasound probe, and adjusting variables such as gain and depth in order to maximize image quality and limit artifact. Performing and interpreting

**Table 4.** Assessment of "Level of Agreement" with Various Statements

| Statement | Pretraining Median | Posttraining Median | Signed Rank | *P*-value | Median of Change From Pretraining to Posttraining | Range |
|---|---|---|---|---|---|---|
| I am *comfortable* with choosing correct probe orientation. | 2.5 | 6 | S(8) = 14 | >0.05 | 3.5 | 6 |
| I am *comfortable* with adjusting depth gain. | 2.5 | 6 | S(8) = 18 | >0.01 | 3 | 4 |
| I am *comfortable* with performing aorta ultrasound exam. | 1 | 6 | S(8) = 18 | >0.01 | 5 | 5 |
| I am *comfortable* with performing the liver/gallbladder ultrasound exam. | 1 | 6 | S(8) = 18 | >0.01 | 4.5 | 4 |
| I am *comfortable* with identifying the anatomy on ultrasound. | 2 | 5.5 | S(8) = 12.5 | >0.05 | 4 | 6 |
| I am *comfortable* with performing the kidney ultrasound exam. | 1 | 5 | S(8) = 10.5 | >0.05 | 4 | 5 |
| I am *comfortable* with performing the cardiac ultrasound exam. | 1 | 5 | S(7) = 13 | >0.05 | 4 | 6 |
| I am *comfortable* with making clinical decisions based on the ultrasound exam. | 2 | 5 | S(8) = 9 | >0.10 | 1.5 | 5 |
| I consider myself *proficient* using the ultrasound for the aorta exam. | 1 | 5 | S(8) = 18 | >0.01 | 5 | 4 |
| I consider myself *proficient* using the ultrasound for the liver exam. | 1 | 4.5 | S(8) = 18 | >0.01 | 2.5 | 3 |
| I consider myself *proficient* using the ultrasound for the kidney exam. | 1 | 4 | S(8) = 14 | >0.05 | 2.5 | 5 |
| I consider myself *proficient* using the ultrasound for the cardiac exam. | 1 | 4 | S(7) = 10.5 | >0.05 | 3 | 6 |

sonographic images requires knowledge of ultrasound physics for accurate image acquisition, which in turn must be appropriately interpreted and then applied correctly to the clinical scenario at hand. The time spent on ultrasound physics for this course was very limited and may have contributed to the decreased confidence providers expressed related to the clinical application of ultrasound. Future courses should invest more time in this important education area. An additional broader reason for the lack of improvement is that that technology is a tool that alone cannot improve clinical decision-making. The hand-carried ultrasound can be used to further the differential diagnosis, but not without a proper history and physical. Regardless, this change in comfort and proficiency is an important step toward future ultrasound education.

The participants expressed that the education experience they valued the most was the hands-on session in which they scanned standardized patients. This is important feedback; however, standardized patients are expensive and alternatives such as simulation may be explored to build tactile skills and eye-hand coordination, as well as to practice the interpretation of normal and abnormal pathology. Prior research has noted that utilization of an ultrasound simulator for training surgical residents and medical students produced posttest results similar to those in resident training with live patients/models.[24,25] The use of ultrasound simulators may prove to be an excellent method for both training and assessment of ultrasound skills.

To help direct further training, it is important to identify the role of hand-carried ultrasounds in family medicine; for example, whether the device will be used for screening or diagnostic purposes. Participants stated that possible indications would be aortic aneurysm screening, ventricular wall thickening, abscesses, foreign bodies, joint injections, and gall bladder pathology. Future training sessions may focus more on abdominal ultrasound, since more participants felt that abdominal ultrasound was important when compared to the cardiac ultrasound.

Participants highlighted problems that may arise with hand-carried ultrasound use, such as billing, certification, medical legal liability, adequate training, lack of probes with different frequencies to allow of imaging of various depths, low usability time due to battery and overheating, and time demand in a clinic. There may be additional concerns with false positive findings and costs that are incurred as a result. These issues may be barriers to adoption of hand-carried ultrasound in family medicine.

## CONCLUSION

In conducting our study, we were unable to identify a standardized, well-validated survey instrument that evaluated these concepts specifically related to hand-carried ultrasound use. Additionally, budgetary constraints limited the sample size of our study. We also were unable to assess the impact of the training on ultrasound skill due to the lack of standardization of the anatomy assessment. Despite the limitations in our study, the objective of the study was to serve as a starting point in the discussion of point-of-care ultrasonography use in family medicine. We believe that point-of-care ultrasonography with hand-carried ultrasounds has the potential to revolutionize how family medicine is practiced, but this cannot be validated without further discussion and research from the family medicine community. The literature reveals little about possible impact on point-of-care ultrasonography in a family medicine setting, which is why we feel it is important to bring this issue into the forefront of the family medicine community. It is important to reiterate that we cannot proceed to evaluate impact of hand-carried ultrasounds or their relative effectiveness compared to more traditional exam techniques without having trained family medicine physicians using hand-carried ultrasounds in the real world.

Our study has helped reveal areas of possible interest and concern in using point-of-care ultrasonography in family medicine. We believe that it is important to encourage further discussion and research from the community to see if point-of-care ultrasonography will affect clinical decision-making and patient cost/benefit in a family medicine outpatient setting.

Further development of the ultrasound-training course will focus on categorizing the indications of ultrasound in a family

medicine setting, addressing the highlighted problems with hand-carried ultrasound use, and creating a long-term training education plan. The ultimate goal of this project is to integrate hand-carried ultrasound education into our family medicine residency so that faculty and residents can use hand-carried ultrasounds in an outpatient setting.

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# Bronchogenic Cyst in the Intradiaphragmatic Location

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## ABSTRACT

Bronchogenic cysts are congenital foregut malformations thought to develop due to abnormal budding of tracheal diverticulum and proximal bronchial structures during embryologic development. The cyst is lined by ciliated pseudostratified columnar epithelium and the wall contains cartilage and layers of smooth muscle. These lesions most commonly are seen in the mediastinum, lung, or pleural spaces. The intradiaphragmatic location of the bronchogenic cyst rarely has been reported in the literature. We report the clinical presentation and computed tomography and magnetic resonance imaging findings in a pediatric patient who presented with left-sided chest pain and was found to have a mass in the region of the diaphragm.


## INTRODUCTION

Bronchogenic cysts are developmental foregut malformations and most commonly are found in the mediastinum close to the tracheobronchial tree. Intradiaphragmatic bronchogenic cyst rarely has been reported. We report an unusual case of bronchogenic cyst in a pediatric patient who presented with left-sided chest pain.

## CASE PRESENTATION

A 13-year-old boy was referred to our hospital with persistent left lower back pain. His history was significant for having been struck by a motor vehicle approximately 1 year earlier. He sustained bruising on the right chest wall due to the impact, and landed on his left side. Imaging at the time of his initial trauma included radiographs of the chest and cervical, thoracic, and lumbar spine. These were all normal. His pain had been constant and was aggravated by deep inspiration. On examination, he was noted to have mild scoliosis of the dorsolumbar spine with tenderness in the lower thoracic area along the left back. No cardiopulmonary or chest wall abnormality was evident on clinical examination. Due to persistent symptoms for 1 year and no relief with physical therapy and chiropractor treatments, cross-sectional imaging was ordered by his primary care physician. A computed tomography (CT) of the chest abdomen was performed that showed a well-defined ovoid hypoattenuating lesion (30-40 HU) centered in the left crus of the diaphragm adjacent to the descending thoracic aorta and fundus of the stomach (Figure 1). There was no calcification or post-contrast enhancement within this lesion. The differential diagnosis included sequestration, ganglioneuroma, or foregut duplication cyst. The patient underwent magnetic resonance imaging (MRI) of the spine for further characterization and evaluation of intraspinal extension of this lesion. MRI revealed mild scoliosis in the dorsolumbar vertebrae with normal appearance of the spinal cord. In addition, there was a well-defined, homogeneous 4.8 x 3 cm, non-enhancing T1 hypointense lesion (Figure 2a & 2b) and T2 hyperintense lesion (Figure 2c) centered in the left crus of the diaphragm. The lesion appeared cystic with a thin wall and small posterior septation. Based on these findings, a foregut duplication cyst was considered the most likely possibility.

The patient underwent a thorocoscopic excision of the cystic lesion (Figure 3). It was covered by diaphragmatic muscle fibers. The pleural surface of the diaphragm was scored and the muscle was cut to expose the cyst, which was filled with mucus. The diaphragmatic defect was closed with interrupted sutures. Notably, the inferior aspect (abdominal surface) of the diaphragm remained intact. The excised cyst was collapsed, measuring approximately 2.4 x 2.0 cm. Microscopically, the cyst was lined by ciliated pseudostratified columnar epithelium (Figure 4). The cyst wall contained lobules of seromucous secretory units, thin layers of smooth muscle, and islands of cartilage. These findings confirmed the diagnosis of bronchogenic cyst. The post-operative course was uneventful and the patient was discharged on postoperative day 2. He was doing well on his postoperative clinic visit, with resolution of his preoperative back pain.

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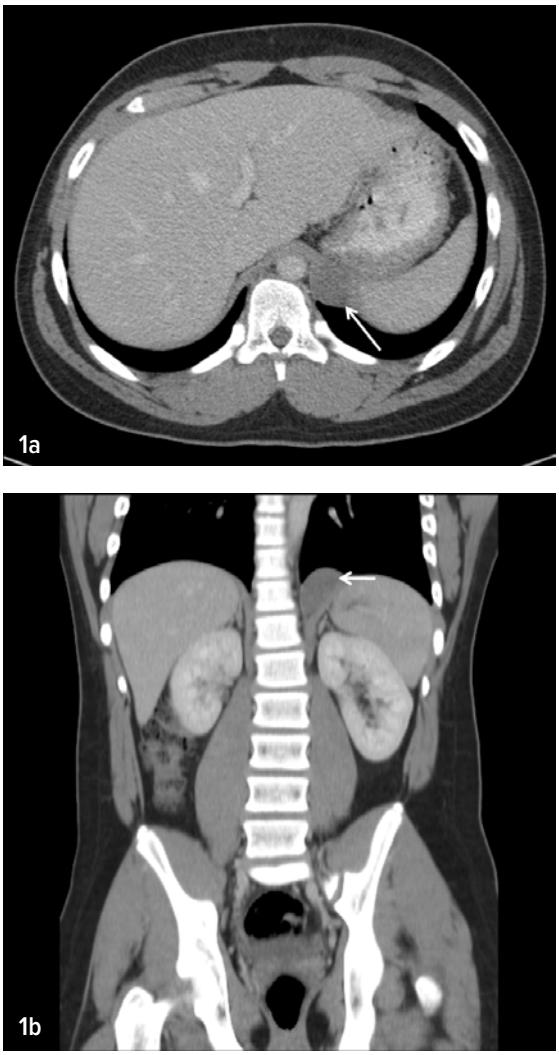
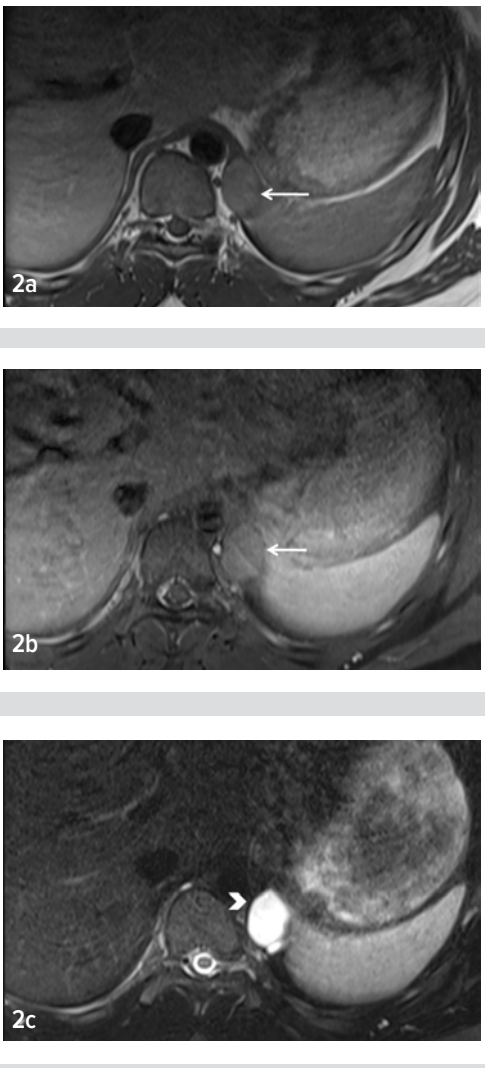
**Figure 1.** Contrast Enhanced CT of Abdomen




Axial image (1a) and coronal image (1b) show an ovoid hypoattenuating non-enhancing lesion (arrow) splitting the left crus of the diaphragm and abutting the stomach.

**Figure 2.** Lesions in the Left Crus of the Diaphragm




T1 axial image (2a) and post contrast T1 axial image (2b) show non-enhancing isointense lesion splitting the leaves of left crus diaphragm (arrow). The cyst is hyperintense (arrow head) on the T2 image (2c) and demonstrates a small posterior septation.

## DISCUSSION

Brochogenic cysts arise from abnormal budding of the tracheobronchial tree during the 26th to 40th day of gestation.[1] They are lined by respiratory epithelium that enlarges due to accumulation of mucus. These cysts also may contain air if they have communication with the tracheobronchial tree.[1] They usually are found in the mediastinum in 85% patients, and 79% occur in middle mediastinum.[1] Mediastinal bronchogenic cysts in newborns and infants can cause respiratory distress due to compression of the airway, and may require surgical resection.[2] Bronchogenic cysts can be associated with other congenital pulmonary malformations like sequestration or lobar emphysema.[3] They also may be found in the lung, pleura, retroperitoneum, and neck.

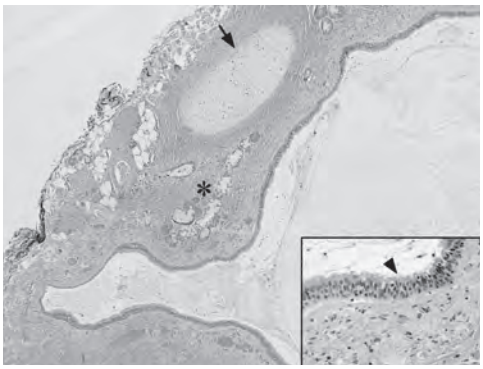
Bronchogenic cysts located within the diaphragm are rare, accounting for less than 30 cases in the English literature. Almost all of these were adults at presentation.[4-6] In a review of 68 patients with bronchogenic cysts, McAdams, et al[1] found only 2 patients with a cyst in the intradiaphragmatic location, both of whom were adults. The only pediatric patient with an intradiaphragmatic bronchogenic cyst was reported by Elemen, et al.[7] They reported a 19-month-old girl who presented with fevers. A chest CT showed a cystic lesion that appeared to be located on segment VIII of the liver. Surgical excision revealed a bronchogenic cyst of the right diaphragm.

Pain was the most common presenting symptom in patients with bronchogenic cyst in most series.[1] However, other presenting symptoms may include fever (due to infection) and symptoms ascribable to pressure on adjacent structures. We believe that the

**Figure 3.** Thorocoscopic Excision of the Cystic Lesion

Intraoperative image shows the cyst (arrow) within the left diaphragm.

**Figure 4.** Microphotographs of the Excised Lesion



The cyst is lined by pseudostratified columnar epithelium. The wall shows lobules of seromucous glands (asterisk), thin layers of smooth muscle and islands of cartilage (arrow). Inset: The columnar cells are ciliated (arrowhead). Hematoxylin and eosin stain. Original magnification x50, inset x400.

chronic back pain in our patient was at least in part related to the bronchogenic cyst. It was brought to clinical attention due to trauma. However, trauma did not have any causal relationship to the development of the bronchogenic cyst.

The CT and MRI findings of bronchogenic cyst have been well described in the literature.[1] They are usually sharply marginated with soft tissue or water attenuation, with cystic characteristics. Some bronchogenic cysts may have soft tissue attenuation, and contrast enhanced CT or MRI may help in distinguishing cystic from solid lesion.[1] Ten percent of bronchogenic cysts can have calcification. In our patient, the lesion had attenuation of 30-40 HU, and showed no enhancement or calcification. On MRI, the lesion was hyper-intense on T2W imaging and did not show any restricted diffusion or post contrast enhancement consistent with cystic lesion. Both CT and MRI demonstrated that the lesion was centered in the diaphragm and appeared to split the crus. Apart from bronchogenic cyst, the differential diagnosis for cystic lesions of the diaphragm include gastrointestinal duplication cyst, cystic pulmonary sequestration, cystic teratoma, mesothelium lined cyst, posttraumatic cyst, or hydatid cyst.[5]

The management of diaphragmatic cyst is surgical excision,[3-6] which establishes the diagnosis and relieves any associated symptoms. Malignant transformation of bronchogenic cysts has been reported.[8] Our patient underwent a thoracoscopic excision of the cyst, which considerably shortened his hospital stay and accelerated his return to full function.

## CONCLUSION

Intradiaphragmatic bronchogenic cyst presenting in pediatric patients with low back pain is rare. Cross-section imaging (CT/MRI) is required when clinical examination and radiographs are unremarkable and the patient's symptoms persist. It should be considered in the differential diagnosis for any cystic lesion of the diaphragm. In this case, the presence of splitting of the leaves of crura by the lesion helped to localize it to diaphragm. Absence of post-contrast enhancement on CT and MRI and lack of restricted diffusion suggested the cystic nature of the lesion. MRI helps to evaluate for the presence of intra spinal extension. Surgical resection is the treatment of choice.

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Elizabeth Petty, MD

Robert N. Golden, MD

# Spencer Foreman, Transformation, and Community Engagement

Elizabeth Petty, MD; Robert N. Golden, MD

The bold vision to transform our school into the nation's first school of medicine and public health in 2005 was sparked by the desire to build an innovative academic infrastructure that would improve the health of all of the people of Wisconsin through the prevention, diagnosis, and treatment of disease.[1] This transformation is an acceleration and expansion of the "Wisconsin Idea," with a lofty goal of serving the entire state through strong community partnerships in education, research, and service.[2]

Over the past 8 years, we have actively transformed all areas of our academic missions and have made substantial progress in fulfilling our vision. In November 2013, the American Association of Medical Colleges (AAMC) recognized our commitment to community engagement with the Spencer Foreman Award for Outstanding Community Service.

Spencer "Spike" Foreman established this award in 1993 during his tenure as AAMC chair, and it was renamed in his honor in 2007. Dr Foreman was a professor at Albert Einstein College of Medicine and served as president of Montefiore Medical Center. He was an inspirational visionary who viewed community engagement and service as an integral part of academic medicine. His namesake award recognizes the academic medical institution that demonstrates "a longstanding, major institutional commitment to addressing community needs" through exceptional programs that reach beyond traditional academic medicine roles into communities whose needs have been unmet through traditional health delivery systems.

Community partnerships, coupled with the resources of the Wisconsin Partnership Program (WPP), have been critical in our transformation to a school of medicine and public health. A cornerstone of our transformation has been dedicated resources from the WPP.[3] The program has supported our efforts to create meaningful research and educational partnerships with communities throughout the state, with the explicit goal of addressing the most pressing health issues and advancing public health through the prevention of disease, injury, and disability.

One key WPP-supported project is the Survey of the Health of Wisconsin (SHOW), directed by Javier Nieto, MD, MPH, PhD. This research program is designed to measure critical health conditions, from well water contaminants to obesity rates, across all of Wisconsin. SHOW will provide a comprehensive picture of the health of our state, and will allow us to identify needs and target resources so that all of our communities become healthier.

Another program that was cited in the Spencer Foreman Award is the County Health Rankings initiative, led by Patrick Remington, MD, MPH.[4] It provides statewide county data that informs health policies that can, in turn, improve the health of citizens around the state, county by county. Based on its initial success in Wisconsin, this initiative received support from the Robert Wood Johnson Foundation to expand to a national program, which now has a major impact across the country.

The Spencer Foreman Award also praised

> There is still much work to be done, and far too many health disparities among disadvantaged communities and populations in our state. We look forward to the next exciting chapters in our ongoing transformation.

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Dr Petty is senior associate dean for academic affairs, University of Wisconsin School of Medicine and Public Health (UWSMPH); Doctor Golden is dean, UWSMPH, vice chancellor for medical affairs, UW-Madison.

our signature programs that are designed to create a physician workforce dedicated to serving underserved rural and urban populations: the Wisconsin Academy for Rural Medicine (WARM) and the Training in Urban Medicine and Public Health (TRIUMPH) programs.[5,6] WARM and TRIUMPH represent an even broader portfolio of academic partnerships across the state with our affiliated campuses at Gundersen Health, the Marshfield Clinic, and Aurora Sinai.[7] These medical student tracks provide dedicated primary care training in medically underserved community settings. A cornerstone of each program is the development of community-based public health improvement projects, which our students pursue in partnership with a wide variety of community programs – from federally qualified health care centers to neighborhood organizations.

In addition to these programs, we have developed educational offerings in global health and public health, which provide students with opportunities to gain hands-on experiences in settings around the world. A recent Human Resources and Services Grant has supported our development of a new "pathway of distinction" for medical and physician assistant students who desire further specialized expertise in public health. A multidisciplinary dual-degree program allows interested medical, nursing, law, pharmacy, and veterinary medicine students to obtain a concurrent master of public health (MPH) degree.

Many of our students embrace community service through a wide variety of extra-curricular activities, which range from the student-run free "MEDiC" clinics for the underserved to volunteer service as health care navigators for pregnant women and as mentors for middle school children. We also have developed rigorous pipeline programs for college students interested in addressing health care disparities as future physicians.

Another key pillar related to these efforts is the Institute for Clinical and Translational Research (ICTR),[8] funded by the National Institutes of Health. This institute is deeply immersed in community engagement through the creation of unique programs such as the Collaborative Center for Health Equity, Health Innovation Program, Health Policy Group, Community-Academic Aging Research Network, Wisconsin Network for Health Research and Wisconsin Research and Education Network. While each of these, as well as other ICTR programs, has a unique focus and mission, they share common goals of engaging community and significantly improving the health of Wisconsin communities. For example, the Collaborative Center for Health Equity works with a variety of rural and urban partners, including tribal partners in Menominee County, to build mutually respectful collaborations designed to increase health equity and improve health outcomes. A thriving partnership between ICTR and the Walnut Way Conservation Corp, a resident-founded nonprofit Milwaukee neighborhood organization, is dedicated to developing targeted programs that will improve the health of that area.

We hope that, in some small measure, we have supported the vision and ideals of Spencer Foreman. We accepted the Spencer Foreman Award for Outstanding Community Service at the AAMC national meeting on behalf of all of our community partners who support the efforts of our students, faculty, and staff. There is still much work to be done, and far too many health disparities among disadvantaged communities and populations in our state. We look forward to the next exciting chapters in our ongoing transformation.

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# MetaStar Project Focuses on Improving Emergency Transfers at Rural Hospitals

Jay A. Gold, MD, JD, MPH

While emergency care is important in all hospitals, it can be particularly critical in rural hospitals, as their distance from fully equipped medical centers frequently necessitates early triage, stabilization, and transfer of patients. In particular, when a patient arrives at an emergency department (ED) needing time-sensitive care that includes transfer to a tertiary care center, the ED's ability to quickly assess, arrange, and move the patient with the necessary and appropriate information can be of life or death importance.

"Many aspects of hospital quality are similar for urban and rural hospitals — for example, providing acute myocardial infarction patients with aspirin," says Eileen Scalise, nurse and quality consultant with MetaStar. "But because of their size, rural hospitals are less likely to provide specialized services such as cardiac catheterization or trauma surgery."

To address the need for seamless transfer communication, MetaStar, the Medicare Quality Improvement Organization for Wisconsin, is partnering with the Wisconsin Office of Rural Health and 18 rural critical access hospitals in the state for a national pilot project that focuses on ED transfers. Wisconsin is one of 8 states participating in the pilot project, which is funded by the Centers for Medicare and Medicaid Services.

The purpose of the Emergency Department Transfer Communication project is to improve performance with regard to 7 domains intended to provide a means of assessing how well an ED communicates key patient information to any receiving health care facility, including communication among physicians at each facility:

- Administrative communication
- Patient information
- Vital signs
- Medication information
- Physician- or practitioner-generated information
- Nurse-generated information
- Procedures and tests

These measures apply to patients with a wide range of medical conditions (heart attack, heart failure, pneumonia, trauma) and are relevant for both internal quality improvement purposes and external reporting to consumers and purchasers.

Data on how well a rural hospital serves this important care transition role are not widely available. The information available often is not standardized for implementation in other EDs. This project will provide each participating hospital with support and training to collect information on transfer communication.

Hopefully, by the project's conclusion, participating hospitals will have strengthened systems and standards of communication that will lead to improvements in the quality of care, safety, and outcomes for patients transferred from rural emergency departments across the state.

The project is time-limited, focusing on cycles of rapid improvement. MetaStar offered critical access hospitals training on the communication tool in October 2013. The hospitals will submit data 3 times, in January, March, and June 2014. In addition to technical assistance and training, MetaStar is offering support for analysis of data reports and development of an action plan to address opportunities for improvement identified by review of CAH results on the measure. Hopefully, by the project's conclusion, participating hospitals will have strengthened systems and standards of communication that will lead to improvements in the quality of care, safety, and outcomes for patients transferred from rural emergency departments across the state.

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Doctor Gold is senior vice president and chief medical officer for MetaStar, Inc. This material was prepared by MetaStar, the Medicare Quality Improvement Organization for Wisconsin, under contract with the Centers for Medicare & Medicaid Services (CMS), an agency of the U.S. Department of Health and Human Services. The contents presented do not necessarily reflect CMS policy. 10SOW-WI-CRSP-13-14.

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