Lung function decline in former smokers and low-intensity current smokers
Kyle Walburg, PharmD
North Memorial Camden Clinic

Background: With more medications for smoking cessation and increased public attention to quitting, there are now more former smokers than current smokers in many developed countries. Overall, current smokers are smoking less cigarettes per day. Studies regarding ongoing lung function decline after quitting yield mixed outcomes; some suggest lung function normalizes after cessation, while others suggest that mechanistically, lung damage could continue.

Objective: This study hypothesized that former smokers and current low-intensity smokers (less than five cigarettes per day) have increased lung function decline as compared to never smokers, including those without prevalent lung disease.

Study Design: Information from six United States population-based cohorts included in the National Heart, Lung, and Blood Institute (NHLBI) Pooled Cohort Study was used in this analysis. Included patients were required to have at least two separate spirometry exams, as validated by American Thoracic Society (ATS) standards; exams were performed between 1983 and 2014. Cohorts included younger adults (17 years and older), middle-aged and older adults (45 years and older), and elderly adults (65 years and older). Lung function decline was measured using forced expiratory volume (FEV$_1$) and compared between former smokers, current smokers, and never smokers. Results were adjusted for sociodemographic and anthropometric factors. FEV$_1$ was also examined with regard to the amount of time elapsed since quitting, cumulative pack years, and current number of cigarettes smoked.

Results: The analysis included 25,432 participants that received at least two valid spirometry exams over the data collection period. Median age of participants was 57 years; FEV$_1$ decline at this median age was 31.01 ml per year [95% CI 30.66-31.37] for never smokers, 34.97 ml per year [95% CI 34.36-35.57] for former smokers, and 39.92 ml per year [95% CI 38.92-40.92] in current smokers. Results were adjusted for former smokers, it was shown that FEV$_1$ decline was accelerated when comparing former smokers to never smokers; the accelerated decline was 20% that of current smokers. Accelerated decline persisted in participants who had quit decades prior and in current smokers with less than ten cumulative pack years.
Low-intensity smokers (less than five cigarettes per day) had 68% that of current smokers smoking 30 or more cigarettes per day, and five times higher than smokers that had successfully quit. It was unclear from the results of this study and other supporting literature if FEV₁ decline decelerates or returns to that of a never smoker after successfully quitting; however, results suggested an accelerated rate of FEV₁ decline persisted decades after quitting smoking.

Conclusions: Smokers that use less than five cigarettes per day or have successfully quit smoking have faster lung function decline compared to those who had never smoked. Importantly, this offers additional evidence about ongoing lung function decline that persists even after quitting smoking. While significant decreases in cigarettes smoked did decrease this rate of decline, even less than five cigarettes per day led to considerable acceleration in lung function decrease. Regardless of if smokers completely quit or decrease their consumption, the results of this study suggest that damage is ongoing and lasting, and progressive lung disease likely occurs. The results of this study help solidify the recommendation that there is no safe level of tobacco smoke exposure, and that smoking cessation is the most efficacious method of harm reduction.

The results can be used to support motivational interviewing performed by pharmacists to influence those attempting to quit smoking. Additionally, the study shows the importance of offering comprehensive care to former smokers, as their risk for ongoing lung decline persists decades after quitting.

Key Point: Former smokers and those smoking less than five cigarettes per day experience faster lung function decline than never smokers. Pharmacists are in a unique position to use results from this study to help facilitate smoking cessation reduce harm.

Summary of DAPA-HF: dapagliflozin in patients with heart failure and reduced ejection fraction²
McKenzie Moore, PharmD
St. Cloud VA

Background: Patients with type 2 diabetes mellitus treated with sodium-glucose cotransporter 2 (SGLT2) inhibitors have been found to have a reduced risk of hospitalization for heart failure in clinical trials. This finding was largely driven by preventing heart failure as the majority of patients included in previous trials did not have a history of heart failure. Although SGLT2 inhibitors were previously untested in this population, patients with a history of heart failure without a diagnosis of diabetes may benefit from the use of SGLT2 inhibitors considering the diuretic and related hemodynamic actions of this medication class.

Objective: Dapagliflozin and Prevention of Adverse Outcomes in Heart Failure (DAPA-HF) was designed to determine if the SGLT2 inhibitor dapagliflozin (Farxiga®) could be used safely and efficaciously in the treatment of patients with heart failure and reduced ejection fraction, regardless of diabetes history.

Study Design: DAPA-HF was a randomized, placebo-controlled trial. Patients were required to have an ejection fraction of 40% or less and meet specified N-terminal pro-B-type natriuretic peptide (NT-proBNP) levels that varied based on history of hospitalization or presence of atrial fibrillation. Those with type one diabetes, symptomatic hypotension or systolic blood pressure less than 95 mmHg, or severe renal disease (eGFR <30 ml/min) were excluded. Patients were stratified based on diagnosis of diabetes. Standard heart failure device therapy such as implantable cardioverter-defibrillator and/or cardiac resynchronization therapy and guideline directed medical treatment were required. For patients with diabetes included in the study, additional glucose-lowering therapies were adjusted if necessary. Due to extensive exclusion criteria, 40% of patients screened did not meet eligibility criteria. A total of 4,744 patients were randomly assigned to receive either dapagliflozin 10 mg daily or matching placebo. The primary outcome was a composite of worsening heart failure (unplanned hospitalization or an urgent visit resulting in intravenous therapy for heart failure) or death from cardiovascular causes. Secondary outcomes also included a composite of worsening renal function and the change from baseline to 8 months in the total symptom score on the Kansas City Cardiomyopathy Questionnaire (KCCQ), a self-administered questionnaire used to evaluate symptoms, limitations, and quality of life in patients with congestive heart failure.

Results: The mean ejection fraction in both treatment and placebo groups was approximately 31% and each group included 45% with diabetes. The primary composite outcome of worsening heart failure or death from cardiovascular causes occurred in 386 patients (16.3%) in the dapagliflozin group and 502 patients (21.2%) in the placebo group (HR 0.74 [95% CI 0.65–0.85] P<0.001). Each component of the primary composite outcome favored dapagliflozin over placebo.
During the median trial period of 18 months, the number needed to treat was 21 patients to prevent one primary event [95% CI 15-38]. Results of total symptom score on the KCCQ were improved in the dapagliflozin group with increase in score of at least 5 points in 58.3% of dapagliflozin patients and 50.9% in the placebo group (OR 1.15 [95% CI 1.08 – 1.23] P<0.001). The composite of worsening renal function did not differ between groups. Safety outcomes were similar in dapagliflozin and placebo groups with 111 and 116 patients discontinuing treatment due to adverse events, respectively (P=0.79). Major hypoglycemia, defined as requiring assistance from another person, was reported in 4 patients in each group and all occurred in patients with diabetes at baseline. Volume depletion related adverse events occurred in 29 (1.2%) dapagliflozin patients and 40 (1.7%) placebo patients (P=0.23). Fournier’s gangrene was also included in the prespecified safety analysis with only one reported case seen in the placebo group.

Conclusions: In patients with reduced ejection fraction heart failure receiving dapagliflozin in addition to standard therapy, risk of worsening heart failure or death from cardiovascular disease is decreased and symptom scores are improved. These benefits are seen regardless of history of diabetes. The mechanism for benefit is still unclear at this time with many possibilities proposed and further research needed. More studies will be necessary to establish a place for SGLT2 inhibitors in heart failure therapy. This trial did not report dosing of standard heart failure therapy to determine if target doses had been reached. Additionally, few patients were included with severe heart failure and subgroup analysis suggests benefit may be less in those with NYHA functional class III and IV compared to class II. Trials currently underway will evaluate the role of other SGLT2 inhibitors in patients with reduced and preserved ejection fraction both with and without diabetes.

Key Point: Regardless of presence or absence of diabetes, dapagliflozin use decreased the incidence of worsening heart failure or death from cardiovascular causes. Although the place in heart failure therapy for SGLT2 inhibitors is not yet defined, pharmacists should be aware of the potential benefit of adding dapagliflozin, particularly for patients with mild heart failure.

Background: Calorie restriction is a known method of weight loss but is often difficult to sustain and associated with rebound weight gain. Intermittent fasting (IF) is an alternate mechanism for weight loss in which eating is restricted to defined periods of time. In addition to weight loss, prior studies have shown that IF can lead to improved glucose metabolism, reduced insulin resistance, and even a lengthened lifespan. However, due to the inconsistent findings of previous studies and varied methods of IF, high quality evidence supporting IF is lacking.

Objective: To explore the effects of IF on weight and glucose metabolism in the general population.

Study Design: This study is a systematic review and meta-analysis in which two investigators selected articles by searching Cochrane, Pubmed, and Embase. Studies were included if they lasted a minimum of 4 weeks. The included population was not pregnant and did not have diabetes mellitus, chronic liver or renal disease. These studies were compared to a control group of studies examining calorie restriction or regular diet. Based on this inclusion criteria, 12 studies (n=545 subjects total) were included in the analysis. The majority of studies included were 8-12 weeks in length, with 3 that were 24 weeks duration. Study participants (61.5% female, 38.5% male) had no differences in BMI or fasting glucose levels at baseline. Statistical analysis was used to determine the weighted mean difference (WMD) between the baseline and post intervention measurements of total body weight, fasting glucose, BMI, fat mass, lean mass, insulin resistance via homeostatic model assessment (HOMA-IR), leptin, and adiponectin.

Results: Eight of the 12 articles reported BMI results; the BMI was lower in the IF group by 0.75 kg/m² [95% CI -1.44 to -0.06; P=0.033]. Total body weight was measured in 10 of the 12 studies and was found to be lower in the IF group but was not statistically significant -1.94 kg [95% CI -5.20 to 1.3; P=0.241]. Eight articles tested fasting blood glucose levels, and the IF group had fasting glucose values reduced by a WMD of 4.16 mg/dL [95% CI -6.92 to -1.40; P=0.003] post intervention. An overall reduction in HOMA-IR by 0.54 [95% CI -1.05 to -0.03; P=0.038] in the IF group was reported in six studies. Lean mass and fat mass did not show significant differences after the IF diet intervention. However, adiponectin levels increased WMD 1008.87 ng/mL [95% CI 140.45-1877.29; P=0.023] while leptin levels were decreased WMN -0.51 ng/mL [95% CI -0.77 to -0.24; P<0.001] in the IF group compared with the control group post intervention.
Conclusions: Overall, this meta-analysis did not show significant reduction in weight with an IF diet. However, a decline in BMI and fasting blood glucose was observed along with an improvement in insulin resistance. Prior studies have shown that an IF diet has a greater impact on those with prediabetes than those without; indicating that an IF diet could show more benefits in those with impaired glucose metabolism. It is important to realize the studies included in this meta-analysis were of a short duration, making it difficult to determine the lasting effects of an intermittent fasting diet. Consider consulting a dietician for their expertise on this topic.

Key Point: Intermittent fasting does not lead to significant weight loss when compared to both calorie restriction and a regular diet, but it has shown to reduce BMI, fasting blood glucose levels, and insulin resistance.

Therapeutic Thought

High-intensity lipid lowering in the elderly population

David Bunch, PharmD
Smiley’s Family Medicine

Background: In 2016 the U.S. Preventive Services Task Force concluded that there is not sufficient evidence to weigh the benefits and harms of statin use for primary prevention in those 76 years and older. The new 2018 ACC/AHA cholesterol guidelines recommend that it is reasonable for patients greater than 75 years of age with clinical ASCVD to receive moderate or high-intensity statin therapy, which differs from their previous 2013 endorsement of only utilizing moderate-intensity statins in this population. Furthermore, the 2018 ACC/AHA guidelines provide a weak recommendation that in adults 75 years of age or older with an LDL-C level of 70 to 189 mg/dL, initiating a moderate-intensity statin may be reasonable. In contrast, the 2014 NICE guidelines recommend for people 85 years or older to consider atorvastatin 20 mg as statins may be of benefit in reducing the risk of non-fatal myocardial infarction. The purpose of this article is to summarize the evidence for using statins in elderly patients.

Evidence: Statins for secondary prevention in the elderly have been well documented in trials such as the PROVE IT-TIMI 22, SAGE, SPARCL, and HPS trials. More specifically, the SAGE trial showed a decrease in all-cause mortality with high-intensity over moderate-intensity statin therapy in those 65-85 years old with coronary artery disease (0.33 [95% CI 0.13 - 0.83]). The recent IMPROVE-IT study determined that adding ezetimibe to simvastatin therapy for secondary prevention resulted in lower rates of their primary endpoint (a composite of death due to cardiovascular disease, myocardial infarction, stroke, unstable angina requiring hospitalization, and coronary revascularization after 30 days) and showed the greatest absolute risk reduction of 8.7% for patients 75 years or older (0.80 [95% CI 0.70 - 0.90]) with no difference found in safety endpoints.

In regards to primary prevention, a retrospective cohort study in Spain by Ramos et al. found that for those aged 75-84 years without diabetes or atherosclerotic disease there was no significant benefit with statin use in either atherosclerotic CVD (0.94 [95% CI 0.86 - 1.04]) or all-cause mortality (0.98 [95% CI 0.90 - 1.05]). However, those with diabetes in this age group saw an improvement in both atherosclerotic CVD (0.76 [95% CI 0.65 - 0.89]) and all-cause mortality (0.84 [95% CI 0.75 - 0.94]). The JUPITER trial tested the effects of high-intensity statin therapy in primary prevention and found that in the population ≥70 years of age, a comparable 39% reduction in risk was found for the combined cardiovascular endpoint of nonfatal myocardial infarction, nonfatal stroke, or cardiovascular death (0.61 [95% CI 0.43–0.86]).

In regards to safety, the JUPITER trial showed no significant difference in muscle weakness, newly diagnosed cancer, or disorders of hematologic, gastrointestinal, hepatic, or renal systems. In this trial, the rates of myopathies were also similar between groups. These results are consistent with other studies such as the SPARCL trial, but slightly different from the HOPE-3 trial which found that more participants in the rosuvastatin group had muscle pain or weakness (5.8% vs. 4.7%, P=0.005).

Discussion and Clinical Impact: As patients get older their risks for having a major cardiovascular event increase, but so do their frailty and risk of adverse events. The 2018 ACC/AHA guidelines provide clearer recommendations for those 75 years or older with clinical ASCVD or diabetes, and new evidence in this area suggests that the addition of ezetimibe to statin therapy in the secondary prevention group may have substantial benefit as well. However, the conversation becomes less clear in the area of primary prevention without diabetes. Studies with subgroup analyses on those 70 years of age seem to show benefit, but meta-analyses with subgroup
Informing your patients about vaping-related lung illness

Taylor Thoof, PharmD
CentraCare – Paynesville

Background: Electronic cigarettes, also known by many names such as e-cigarettes, e-cigs, vape-pens, or vapes, have recently been linked to multiple cases of severe respiratory illness across the United States. The use of such devices is often known as vaping. E-cigarettes contain liquids, known as e-liquids, that are heated by a battery-powered device to form an aerosol, often incorrectly referred to as vapor, which is then inhaled. These liquids can contain various substances such as nicotine, propylene glycol, vitamin E-acetate, vegetable glycerine, formaldehyde, tetrahydrocannabinol (THC), and flavorings. The individual components can vary greatly between products. While some of these individual substances have been evaluated to be safe to ingest, there is inconclusive data supporting their safety when inhaled. Additionally, the use of e-cigarette products has recently been associated with severe lung disease, with over 2,000 reported cases and 39 deaths as of November 5th, 2019. E-cigarette or vaping use associated lung injury (EVALI) may present with various non-specific symptoms such as cough, shortness of breath, chest pain, abdominal pain, nausea, vomiting, diarrhea, fever, chills, or weight loss. Little is known about specific toxicants in EVALI at this time, but a majority of cases report that patients utilized e-cigarettes containing THC. Recent reports from the Centers for Disease Control (CDC) suggest that a vitamin E-acetate, an additive in off-market e-liquids, may be a primary intoxicant in EVALI.

Evidence: Data from Song and colleagues suggests that use of even flavorless and nicotine free vaping liquids may result in lung inflammation. In a four-week, pilot trial, 30 individuals classified as never-smokers (smoked less than 100 cigarettes in their lifetime) were randomized to either e-cigarette use or no use controls. Individuals randomized to e-cigarette use were provided with identical devices and provided with an e-liquid containing 50% propylene glycol and 50% vegetable glycerine. Subjects underwent bronchoscopy and bronchoalveolar lavage (BAL) at baseline and at five weeks to assess inflammatory cell counts and cytokines. Adherence to study protocol was assessed via urinary propylene glycol concentrations and patients recording daily puff counts from their e-cigarette. There was no statistically significant difference in BAL inflammatory cell counts or cytokines between groups at baseline and at five weeks. However, investigators observed that change in urinary propylene glycol from baseline was significantly correlated with change in cell counts, R=0.60, P=0.03. Investigators did note that overall changes were small in this trial, but they noted that the short duration of the study as a limiting factor for assessing the effect of chronic e-cigarette use may have on pulmonary tissue.

While data from controlled trials are lacking at this time, the CDC has reported in early November 2019 that it believes that the substance vitamin E-acetate may be associated with EVALI based on bronchoscopy and bronchoalveolar lavage (BAL) samples from confirmed EVALI cases. Vitamin E-acetate is a diluent commonly used in e-liquids containing THC. Of twenty-nine bronchoscopy and BAL samples sent to the CDC from across the United States, all twenty-nine samples contained vitamin E-acetate. THC was detected in twenty samples and nicotine metabolites were
Another CDC report detailed differences in e-liquid formulations prior to and after the EVALI outbreak in 2019. The Minnesota Department of Health (MDH) tested ten e-liquid formulations that were seized in 2018 against twenty e-liquid formulations seized in September, 2019. All of these formulations all contained THC and were intended for sale on the illicit market. It was determined that all twenty products seized in 2019 contained vitamin E-acetate, but none of the ten products seized in 2018 contained vitamin E-acetate.

Discussion: Data from controlled trials on the safety of inhaling aerosols of various components in e-cigarettes is sparse at this time. While certain products such as such as propylene glycol and vegetable glycerine have previously defined acceptable levels for human consumption and cosmetic use, the safety of these products when heated and inhaled via an aerosol may vary as demonstrated by Song and colleagues. Song and colleagues propose that the use of e-cigarettes containing propylene glycol moderately correlates to lung inflammation. Propylene glycol is a common excipient in e-liquids and therefore there is a potential risk for lung inflammation with use of most e-cigarettes. In regards to serious lung damage due to EVALI, the CDC hypothesizes that vitamin E-acetate is the primary intoxicant, and not other excipients. This belief is driven by the majority of BAL samples from confirmed EVALI cases containing vitamin E-acetate and the discovery that e-cigarette formulations containing are a fairly recent development.

The existing data provided from the CDC does not present enough evidence to establish a causal relationship between the presence of vitamin E-acetate and EVALI, but a correlation does seem to exist. While this finding is promising in identifying a potential toxicant linked to EVALI, further studies are needed whether a causal relationship exists between EVALI and vitamin E-acetate.

Clinical Impact: While there is much to learn about EVALI, pharmacists have the opportunity to share basic information with their patients to promote safety. At this time, the CDC recommends that individuals should refrain from buying any type of e-cigarette product but especially recommend avoiding THC containing products. It is believed that vitamin E-acetate may be a potential toxicant, but there is inconclusive data at this time. Patients who have been utilizing e-cigarettes for smoking cessation should be advised not to go back to not to go back to smoking but instead consider using other evidence-based treatments for smoking cessation. For patients interested in quitting their use of e-cigarettes, pharmacists should also recommend the same evidence-based treatments to assist in quitting. If individuals continue to use e-cigarettes, it is advised that they continually monitor for symptoms associated with EVALI and seek medical attention if these symptoms develop. Pharmacists should advise that patients experiencing cough, shortness of breath, chest pain, abdominal pain, nausea, vomiting, diarrhea, or fatigue and have used e-cigarettes within the past ninety days to seek out further medical attention.

2019 CAP Guidelines Update19-20
Kylea Larsen, PharmD
Coborn’s Pharmacy/Little Falls Family Medical Center

Background: The American Thoracic Society (ATS) and Infectious Diseases Society of America (IDSA) has released updated guidelines for the diagnosis and treatment of adults with community-acquired pneumonia (CAP). The 2019 ATS/IDSA CAP guidelines address 16 specific areas of CAP treatment and give recommendations using evidence-based rationale. Compared to the 2007 ATS/IDSA CAP guidelines, many recommendations are unchanged but there are some notable differences in the 2019 update. The major changes found in the 2019 guidelines include identification of patient populations for sputum and blood culture draws, utilization of the term “healthcare-associated pneumonia (HCAP),” treatment with macrolide monotherapy, and empiric therapy recommendations for severe CAP.

Evidence: The 2019 ATS/IDSA CAP guidelines continue to recommend the use of sputum cultures and blood cultures in patients with severe disease managed in the hospital and recommend against the routine use of sputum cultures and blood cultures in the outpatient setting for adults with CAP. Additionally, the updated guidelines specify that sputum cultures and blood cultures should be obtained in patients who are empirically treated for Methicillin-resistant Staphylococcus aureus (MRSA) or Pseudomonas aeruginosa in the hospital due to specific risk factors for infection. These risk factors include previous infection with MRSA or P. aeruginosa or hospitalization that resulted in the use of parenteral antibiotics within the last 90 days.

A term previously used to guide selection of antibiotic
THERAPEUTIC THOUGHT (cont.)

therapy was abandoned in the 2019 CAP guidelines.

Introduced in previous guidelines, HCAP was a term used for patients who were not hospitalized but thought to have risk factors for antibiotic-resistant pathogens due to various exposures to the healthcare system. The new recommendation is to classify these types of risk factors as CAP. Additionally, it is recommended to cover for MRSA or P. aeruginosa only if local risk factors for the pathogens exist. This recommendation requires more research into site-specific data and was based on the increasing use of extended-spectrum antibiotics to treat MRSA and Pseudomonas despite the generally low prevalence of infection at individual sites.

Another update to the 2019 ATS/IDSA CAP guidelines involves specific pharmacological therapy recommendations. The use of macrolide monotherapy for adults diagnosed with CAP in the outpatient setting was changed from a “strong” recommendation to a “conditional” recommendation based on local resistance patterns. Macrolides are recommended as monotherapy for healthy patients without comorbidities and a local pneumococcal resistance to macrolides <25%. This recommendation is based on evidence of macrolide failures that occurred due to the macrolide-resistant Streptococcus pneumonia and a macrolide resistance rate >30%.

Additionally, the recommendation for standard empiric therapy of severe CAP in the inpatient setting was updated. The 2007 guidelines recommended the use of either a β-lactam/macrolide combination or a β-lactam/fluoroquinolone combination. The 2019 guidelines state that both combinations are still acceptable, but there is now stronger evidence available that favors the β-lactam/macrolide combination. The evidence used for this recommendation includes two meta-analyses of observational studies. Therefore, the guidelines indicate more research is needed.

Discussion and Clinical Impact: Many recommendations found in the 2019 ATS/IDSA CAP guidelines were unchanged from the previous guideline. However, specific updates around diagnosis and treatment recommendations were highlighted. The new guidelines will help providers order appropriate tests and medication therapies for patients based on risk factors and diagnoses and therefore increase antimicrobial stewardship. Further updates beyond the major changes covered in this article can be found in the 2019 ATS/IDSA CAP guidelines.

FROM THE PHARMACY PRESS

Community Pharmacy Enhanced Service Network (CPESN®) now in Minnesota21-23
Alison Kingsbury, PharmD
GuidePoint Pharmacy

Background: This past September, 31 community pharmacies founded Community Pharmacy Enhanced Services Network (CPESN) Minnesota. Striving for a higher level of care, CPESN is an integrated network of community pharmacies that coordinate patient care to provide medication optimization activities and enhanced services. Enhanced services of community pharmacies in CPESN may include: face-to-face access for patients, medication reconciliation, clinical medication synchronization, comprehensive medication reviews, personal medication records, collection of vital signs, tobacco cessation program, point of care testing, administration of long-acting injectables, naloxone dispensing, and nutritional counseling.

In 2014, the first Community Pharmacy Enhanced Services Network was initiated when the Community Care of North Carolina (CCNC) established the first network in North Carolina; capitalizing on community pharmacies regular encounters with those in the community requiring a higher level of care. North Carolina Medicaid claims, according to CCNC, revealed patients with the most need of medication-focused care coordination visit the pharmacy more than thirty-five times annually contrasted to three and a half visits to their primary care provider. Increased patient encounters enable community pharmacies to grow to be an integral part of health care teams to improve patient outcomes.

Evidence: Community pharmacies influence outcomes associated with reducing readmissions to the hospital, enhancing the value of medication, and improving patient satisfaction. Per a CCNC performance analysis of CPESN North Carolina, high-risk Medicaid patients working with their primary care provider and supported by a CPESN pharmacy were: 45% less likely to have an inpatient hospital admission; 35% less likely to have preventable hospital admission or readmission; 15% less likely to an emergency department visit; 25% more likely...
Primary care underwent change to outcomes-based reimbursement by creating Accountable Care Organizations (ACO) and now pharmacy, through CPESN, is striving to create accountable pharmacy organizations. With health care shifting to outcomes-based reimbursement, CPESN’s emphasis on enhancing patient outcomes align with other members of the health care team.

Enhanced services in the community pharmacy have also demonstrated to reduce health care costs. Towncrest Pharmacy, a pharmacy in CPESN Iowa performed a pilot study with a payor to illustrate the cost benefit of patients utilizing a pharmacy with enhanced services. Over a one-year period, total health care costs were compared between patients that utilized Towncrest Pharmacy for: all prescriptions, about 50% of prescriptions; or do not fill prescriptions at Towncrest Pharmacy. The patients that filled all prescriptions at Towncrest Pharmacy used $298 and $309 less than those who do not fill at the enhanced services pharmacy (N=546, P<0.0001) and who filled 50% of the time at the pharmacy (N=340, P<0.0012), respectively. Showing lower health care costs when patients utilize an enhanced service pharmacy incentivizes payors to change the pharmacy reimbursement model.

Clinical Impact: CPESN Minnesota has embarked on a two-year grant with other states’ CPESN to transform pharmacy practice to focus on enhanced services. These pharmacies aim to demonstrate the benefits of community pharmacies’ outcomes on a large scale. Pharmacies document the outcomes through care plans to demonstrate to payors the benefit of an accountable pharmacy organization. CPESN Minnesota endeavors to create new practice of community pharmacy that is an integral part of the healthcare team.

Type 1 Diabetes Mellitus Treatment Options: is there more than just insulin?24

Kaylin Maddy, PharmD
Park Nicollet Health Services

Background: Treatment of type 1 diabetes mellitus (T1DM) is mostly dependent on the use of insulin. Less than 30% of patients with T1DM meet glycemic targets, largely limited by wide fluctuations in glucose levels and inability to further escalate insulin doses due to hypoglycemic episodes. Additionally, obesity rates are greater than 50% in those with T1DM, in many cases due to long-term insulin use. Glucagon-like peptide 1 receptor agonists (GLP-1 RA) have been a highly valued addition to the treatment of type 2 diabetes mellitus (T2DM), without the weight gain or hypoglycemia common to insulin. Interestingly, GLP-1 RA’s also address a gap in the current available treatment options for T1DM by targeting alpha cell dysfunction and potentially disease progression.

Evidence: It is thought that GLP-1 RA work in T1DM by suppressing glucagon secretion from alpha cells, increasing satiety, and having insulinotropic effects. Of the GLP-1 RA’s, considerable data only exists for exenatide and liraglutide in T1DM. Exenatide evidence is limited, with only three studies looking at the immediate release formulation and one small study looking at extended release. The first immediate release exenatide study was a one day study looking at eight adolescent patients, which found significant reductions in postprandial hyperglycemia and delayed gastric emptying. The second study looked at 20 individuals with longstanding T1DM and found a significant decrease in weight and total daily insulin needs, but no significant findings for A1C or endogenous insulin production. They hypothesized the insignificant findings could be attributed to the fact that exenatide did not have insulinotropic effects in those with longstanding disease and complete insulin deficiency. The final study looked at 18 patients with newly diagnosed T1DM and detectable C-peptide. They found a significant decrease in insulin requirements and weight, and a non-significant increase in C-peptide levels.

For extended-release exenatide, a retrospective study looked at 11 individuals. While they did find significant reductions in weight, insulin needs and A1C, they noted 45% of patients discontinued therapy by 6 months due to intolerance of injection site nodule formation or gastrointestinal intolerance. Liraglutide has more comprehensive evidence to support its use in T1DM, with nine studies in total.

Overall, the studies showed no increase in C-peptide levels in both patients with detectable and undetectable levels at baseline. They found a mean A1C reduction of 0.23% for 1.2 mg daily dose and 0.8% for 1.8 mg daily dose. The overall weight decrease was 4 to 5.9 kg from baseline on maximum dose liraglutide. Weight and A1C effects were both more prominent in patients with detectable C-peptide levels. Observed rates of hypoglycemia with liraglutide in T1DM were similar to the use of liraglutide used in combination with sulfonylureas in T2DM, however this was with a 25-50% empiric insulin dose reduction.
Discussion: Overall for exenatide, the most encouraging findings are for the use of the immediate release formulation in patients with newly diagnosed T1DM. However due to small sample sizes in the few available studies, further research is recommended before implementing its use in clinical practice. Liraglutide has a greater amount of available evidence to support its use, however clear recommendations for its use in T1DM are still unknown. GLP-1 RA’s, specifically exenatide and liraglutide, may be a future new tool for add-on therapy in patients with T1DM seeking a reduction in insulin doses, weight loss, or modest improvements in A1C. The beneficial effects are more pronounced when C-peptide is detectable, potentially due to lack of insulinotropic effects when undetectable. The modest improvements in A1C should be noted, however, it should be recognized that the addition of GLP-1 RA occurred in combination with significant insulin dose reductions likely contributing to this modest finding. There does not appear to be a significant increased risk of hypoglycemia, though empiric insulin dose reductions should be followed. Further research is needed to evaluate the use of dulaglutide and semaglutide for patients with T1DM. Additionally, the effects on microvascular and macrovascular complications need to be further explored.

Clinical Impact: The use of GLP-1 RA’s may be an exciting future tool for individuals with T1DM, more likely to benefit those with detectable C-peptide, weight above goal, or struggling with hypoglycemia on insulin therapy. However, there is not currently enough conclusive evidence to support their use in practice.

Evidence: A total of 29 studies and meta-analyses evaluating the safety and efficacy of various therapeutic regimens in specific patient populations were included in the review by Nguyen et al. Per the 2017 ACG guidelines on treatment of H. pylori infection, first-line therapy for the general population includes either clarithromycin triple therapy (clarithromycin, amoxicillin or metronidazole, and a proton pump inhibitor (PPI)), bismuth quadruple therapy (bismuth salt, PPI, tetracycline, and metronidazole or amoxicillin), or triple antibiotic therapy (clarithromycin, amoxicillin, metronidazole, and PPI).

For patients with a confirmed penicillin allergy, ACG guidelines recommend clarithromycin triple therapy with metronidazole. For patients with recent macrolide exposure, bismuth quadruple therapy with metronidazole is preferred due to the risk of harboring clarithromycin-resistant H. pylori. If the patient has other contraindications or fails either first-line regimens, a second-line therapy containing levofloxacin has favorable eradication rates.

For patients with, or at risk for developing, a prolonged QTc-interval, therapies containing clarithromycin or levofloxacin may not be preferred. In these situations, bismuth quadruple therapy is the recommended regimen. In patients who have failed or are unable to tolerate bismuth quadruple therapy, the second-line regimen of choice is amoxicillin dual therapy.

In asymptomatic patients who are pregnant or breastfeeding, it is recommended to delay treatment until delivery or cessation of breastfeeding due to lack of safety data for any of the regimens. In symptomatic patients, such as those with hyperemesis gravidarum, a risk vs. benefit conversation with the patient must occur. If the decision to pursue treatment is made, clarithromycin triple therapy is recommended. In elderly patients with an H. pylori infection, special attention must be made for potential drug-drug interactions, appropriate drug dosing, and adverse drug monitoring. The first-line treatment recommendations remain the same as for the general population. Additionally, both clarithromycin and levofloxacin require renal dose adjustments.

Discussion: Recommended therapy for the treatment of H. pylori infection widely varies depending on patient-specific factors. Due to the complexity of these regimens and the importance of complete infection eradication, providers must ensure careful consideration be made to ensure optimal tolerability, safety, and efficacy.

Treatment of Helicobacter pylori in Special Patient Populations 25-26
Andrea Richard, PharmD
Anoka Metro Regional Treatment Center / Minnesota Direct Care and Treatment

Background: Helicobacter pylori infection is a common cause of gastritis, gastric and duodenal ulcers, and gastric cancer. Due to the morbidity associated with these infections, complete eradication of the bacteria is the goal of therapy. Treatment guidelines from the American College of Gastroenterology (ACG) include first-line and salvage regimens consisting of antibiotics and at least one antacid agent. A review of the new guidelines written by Nguyen et al discussed the current evidence for H. pylori treatment selection in special populations.
Pharmacists in California can now dispense PrEP for HIV prevention without a prescription
Vicky Wongbi, PharmD
Community University Health Care Center (CUHCC)

Legislation signed by Governor Gavin Newson in September 2019 marks a milestone in the health of Californians. California is the first state in the country to authorize pharmacists to dispense Human Immunodeficiency Virus (HIV) pre-exposure prophylaxis (PrEP) and post-exposure prophylaxis (PEP) without a prescription. This was an effort, as seen by proponents in removing the barriers that exist in obtaining PrEP and PEP, which are highly efficacious in the prevention of the spread of HIV infection. PrEP is a way for people who do not have HIV but who are at very high risk of getting HIV to prevent HIV infection by taking an antiretroviral pill every day. PEP means taking antiretroviral medicines after being potentially exposed to HIV to prevent becoming infected. PEP is used only in emergency situations and must be started within 72 hours after a recent possible exposure to HIV.

Like most new laws, this advance was not without concerns. The California Medical Association originally opposed this bill, citing concerns for inappropriate use and lack of monitoring. To address this concern, the legislature limits the number of PrEP pills a patient can get without a prescription to a maximum of 60 days. In conjunction, this legislation prohibits insurance companies from requiring a PA to receive PrEP. This will further eliminate some of the barriers individuals may face in obtaining PrEP medication.

This legislation is evermore expanding the scope of practice for pharmacists. Pharmacists are considered valuable members of the healthcare team and by expanding their role, certain medications can become more accessible to patients who have trouble obtaining medications. For example, pharmacists in many states are already dispensing other medications without a prescription, including naloxone and emergency contraceptives. This expansion of the profession promotes patient access to medications and healthcare.

Descovy: The new era of HIV prevention
Anh Nguyen, PharmD
Walgreens / Bethesda Family Medicine Clinic

Although healthcare has made tremendous strides throughout the years, over 38,000 people were diagnosed with human immunodeficiency virus (HIV) in 2017. Since the discovery of HIV in the early 1980s, several HIV treatments have come out on the market, however, only TruvadaTM has been indicated for HIV prevention, until now. Recently in October of 2019, the U.S. Food and Drug Administration (FDA) approved Descovy™ as pre-exposure prophylaxis (PrEP) to reduce the risk of acquiring HIV type 1 (HIV-1). Descovy™ is only FDA approved for adults and adolescents weighing > 35 kg and excludes individuals at risk of HIV-1 infection from receptive vaginal sex.

In a randomized, double-blinded multinational trial in 5,387 HIV-negative men and transgender women, the rate of HIV-1 infection was similar between participants who were taking Descovy™ with those who were taking TruvadaTM. Both Descovy™ and TruvadaTM contain emtricitabine. However, Descovy™ also contains tenofovir alafenamide while TruvadaTM contains tenofovir disoproxil fumarate. The tenofovir disoproxil fumarate component in TruvadaTM has more side effects as well as renal adjustments with CrCl < 50 ml/min and more long-term bone demineralization than Descovy™ which only warrants discontinuation at CrCl < 30 ml/min. Both medications have a black box warning for exacerbating hepatitis B (HBV) infections in people infected with HBV.

Descovy’s™ new FDA indication expands HIV prophylaxis to a much wider patient population such as those with renal dysfunction like our elderly population and patients who could not tolerate TruvadaTM side effects. With this new expansion, we’ve stepped into a new era of HIV prevention that can help lead us to defeat the HIV epidemic.

Personalizing treatments for antidepressants and antipsychotics
Anh Nguyen, PharmD
Walgreens / Bethesda Family Medicine Clinic

In 2017, 17.3 million adults in the United States reported at least one major depressive episode, making it the leading cause of disability. Resistant depression not only is a burden to patients and their families, but also is a financial strain to the healthcare system.

UnitedHealthcare recently announced a new coverage policy for multi-gene panel testing for antipsychotic and antidepressant medications that became available starting October 1st, 2019. This new policy includes coverage for use of pharmacogenetic multi-gene
panels to guide clinical decisions on medication if the individual has a diagnosis of major depressive disorder or anxiety, has failed at least one prior medication to treat their condition and multi-gene panel has no more than 15 relevant genes.

UnitedHealthcare’s new policy was guided by evidence from the GUIDED study published by the Journal of Psychiatric Research. This randomized controlled trial included more than 1,100 participants with depression who either received treatment guided by GeneSight, a pharmacogenomics test, or by conventional treatment methods without GeneSight guidance. Participants in the GeneSight group rate of admission at eight weeks were 50% higher than those in the conventional treatment group. Additionally, individuals in the Genesight group had a 30% higher rate of response and 11% greater improvement in symptoms. Other studies have demonstrated that using GeneSight saves $6,050 per patient in the first-year of healthcare costs and reduces disability claims and medical absence days. UnitedHealthcare’s new coverage policy would not only benefit their customers but also the healthcare system itself. Personalized medicine would help patients achieve remission quicker, potentially reducing hospitalization rates, healthcare cost and risk of patient relapse.

REFERENCES