SDSHP NEWSLETTER

Message from the President and President-elect

SDSHP is excited to kick off our very first edition of the SDSHP newsletter! The goal of the newsletter is to keep membership connected with the SDSHP activities and to share stories of Pharmacy Practice Advancement successes. We'll also include different sections throughout the year to allow contributions from members of SDSHP and students from the SDSU College of Pharmacy.

Last May, SDSHP hosted a South Dakota Pharmacy Practice Model Initiative (PPMI) State Affiliate Workshop. Some opportunities that were discussed included increasing awareness of progress different practice sites and pharmacists have made across our rural state. Since the workshop has taken place, ASHP has changed the name of the initiative from Pharmacy Practice Model Initiative to Practice Advancement Initiative (PAI). The change was made to embrace and reflect a broader range of pharmacist services and care settings.

SDSHP is working to promote the PAI in South Dakota by sharing experiences in the newsletter pharmacist spotlight section and at the 2016 Annual Meeting.

Pharmacist Practice Spotlight

This issue's spotlight is on: Steven Lee, PharmD; Director of Clinical Services; Avera Medical Group-Pierre.

Please describe your practice site (clinic, hospital, community, etc)

Avera Medical Group-Pierre, a 45-Provider, multi-specialty ambulatory clinic location owned by Avera, now associated with Avera St. Mary's Hospital in Pierre.

Initially, my activities started out with a collaborative practice between our Medical Staff and myself, largely restricted to patient care visits relative to Cardiovascular Risk Reduction. This included anticoagulation management as well as lipid management and ambulatory blood pressure monitoring. Shortly after initiation, another collaboration occurred between the Clinic and the SDSU College of Pharmacy. I served as an Assistant, then Associate Professor of Clinical Pharmacy for SDSU with an active Ambulatory Care rotation site for approximately 8 years. Eventually, a move toward conducting Clinical Trial activity involving Phase III and IV investigational drugs took the place of the time available to work with the College, leading to my resignation with SDSU. A number of SDSU students continue to spend short amounts of time visiting my practice site now. After serving as the Interim Clinic Administrator for some time in 2011, my job description was refined to Director of Clinical Services for the Clinic where I now assist in most Provider-related Clinical Program development activities, as well as continuing to run a fairly vigorous anticoagulation service for our outpatients.

Please describe what makes your practice site unique and innovative.

Established in January, 2001, the Medical Associates Cardiovascular Risk Reduction Clinic (name prior to Avera purchasing) was the first, non-VA/non-IHS Pharmacist-run collaborative Pharmacotherapy Clinic that I am aware of that was conducting fee-for-service Pharmaceutical Care. At the time, outpatient Pharmaceutical Care was just getting rolling. Pending legislation in the US Senate, heavily influenced by our previous Dean of the SDSU College of Pharmacy, Brian Kaatz, promised great things for the recognition of Pharmacists as providers by Medicare. I was just completing my non-traditional Pharm D through Creighton University at the time and had an excellent relationship with some local Physicians, who suggested that we give the collaborative effort a try. I guess that is the "innovative" part.

Fortunately for the health of our Country, my site is no longer "unique", but rather, somewhat common. That is wonderful for Pharmacists, and

Guideline updates

CHEST issues new antithrombotic guidelines for the treatment of VTE disease.

Key changes:

- Non-vitamin K antagonist oral anticoagulants are suggested over warfarin for initial and long-term treatment of VTE in patients without cancer. Since publication of the 9th edition, new studies show that non-vitamin K antagonist oral anticoagulants are as effective as VKA therapy with reduced risk of bleeding and increased convenience for patients and health-care providers
- Patients with unprovoked proximal DVT or PE who are stopping anticoagulation should receive aspirin to reduce the risk for recurrent VTE, assuming aspirin is not contraindicated.
- Patients with low-risk PE may be treated at home or receive an early discharge

See the full guidelines at:

https://www.chestnet.org/Guidelines-and-Resources/Guidelines-and-Consensus-Statements/Antithrombotic-Guidelines-9th-Ed

also wonderful for patients. After almost 15 years of practice in this site, however, one thing stands very clear: The applications of a Clinic Pharmacist in all Ambulatory Care settings are many. Practice sites that do not have this service available to their Providers and patients do not know what they are missing. Those sites that have had the luxury would likely say that they would care not to practice without that service available. This has nothing to do with me or my abilities, but rather, the significant application of folks like us in this environment. There is so much to do, so many places to help, etc.

Please provide any guidance for practitioners looking to set up a similar practice.

Collaborate. Collaborate with Physicians, collaborate with Advanced-Practice Providers, Nurses, Lab staff....everybody! Once these folks realize that you are augmenting their practices, rather than a threat (competition), you will be welcomed with open arms. While MTM and other Clinical Pharmacy Activities can be performed "outside" of the normal Clinic environment, I see very little value in trying to actively manage a patient's medication therapy without unfettered access to the complete medical record. That is really only available to use through our collaboration with the Providers that take care of these folks. To do our best, we need ALL of the information relative to our patients...not just what shows up on their medication list at the Pharmacy or is provided by them verbally.

What are your biggest challenges?

Provider status by Medicare....like everybody else's largest challenge. I think that we've proven that we can do this without it, although our ability to generate enough productive income to offset the expense of our salaries requires Clinic Administrators and collaborating Physicians to really think outside the box. Should we ever reach that milestone with Medicare, then have private insurance companies follow their lead, Clinical Pharmacists could be as common in Ambulatory Clinic settings as the front desk.

What were your biggest successes?

Initially, it was the slow process of winning the confidence of many of the more "tenured" Medical Staff for which I worked. That took time, but was extremely rewarding once it had taken root. Success with patients came easy. They were hungry for services such as this and generously let us know that we were providing something of value to them. They continue to do that today.

Eventually, my biggest successes took the form of the relationships that developed between my Colleagues and me.....Professors, Pharmacists and Physicians. It was further enhanced by the many pharmacy students with whom I became acquainted over that 8 years of vigorous teaching, but still today to a lesser degree. They often taught me as much as I taught them....once I became humble enough to accept it.

Journal Club: by Luke Klugherz, PharmD Candidate

Empagliflozin, Cardiovascular Outcomes, and Mortality in Type 2 Diabetes (EMPA-REG OUTCOME)
Zinman B, Wanner C, Lachin JM, et al; EMPA-REG OUTCOME Investigators. N Engl J Med. 2015 Sep 17.

Background
Cardiovascular disease and diabetes increase the risk of death, and evidence is conflicting whether or not glucose-lowering agents are beneficial for the cardiovascular system and mortality. Sodium-glucose cotransporter 2 (SGLT2) inhibitors such as empagliflozin (Jardiance) have been used as monotherapy or adjunctively to decrease glucose levels and A1C in diabetic patients (including those with kidney disease). However, their cardiovascular benefits are relatively unknown.

Objective
Examine the effects of empagliflozin (compared with placebo) on cardiovascular morbidity and mortality.

Endpoints
1° Composite: death from CV cause, nonfatal MI (excluding silent MI), nonfatal stroke
2° Composite: primary endpoint plus unstable angina hospitalization

Safety
AEs during treatment or within 7 days of last dose of study drug: hypoglycemia, UTIs, genital infections, volume depletion, acute renal failure, bone fractures, DKA, thromboembolic events

Study Design
Randomized, double-blind, placebo-controlled trial with 1:1:1 treatment arms of empagliflozin 10 mg, 25 mg, or placebo at 590 sites throughout 42 countries. The study was continued until the primary outcome occurred in at least 691 patients (average duration of 3.1 years) to achieve 90% power. Two-week open-label placebo run-in period (before randomization) featuring unchanged glucose-lowering therapy. Original glucose-lowering therapy also unchanged for first 12 weeks after randomization unless fasting glucose was >240. Investigators were encouraged to treat diabetes and cardiovascular conditions per "local guidelines."

Inclusion Criteria
- Adults ≥ 18 years
- CrCl ≥ 30 mL/min
- BMI ≤ 45 kg/m²
- Established CV disease (CAD, PAD, history of stroke/MI, etc.) and:
    - A1C 7-9% if no glucose-lowering agents administered for at least 12 weeks prior to study
    - A1C 7-10% if glucose-lowering agents administered for at least 12 weeks prior to study

Population
- 7,020 patients, very similar characteristics between treatment arms
- 71% males; 55% <65 years
- 99% with pre-existing CV disease, 95% receiving BP therapy
- 61% had BP < 140/90
- 69% had initial A1C<8.5%
- 74% had GFR >60 mL/min

Statistical Analysis
Four-step hierarchal-testing using two-sided P value of ≤ 0.0498 for significance: primary outcome non-inferiority, secondary outcome non-inferiority, primary outcome superiority, secondary outcome superiority. 90% power at 691 events. Modified intention-to-treat analysis. Cox proportional-hazards model utilized for outcome analysis; Kaplan-Meier estimate for all-cause death.

Results
Safety:
- Significantly lower rates of death and overall/severe AEs in empagliflozin
- Significant lower acute renal failure and AKI rates in empagliflozin
- Significantly lower UTI rate in females in empagliflozin (no significant difference in men)
- Significantly increased incidence of genital infections in empagliflozin (men and women)
- No significant hypoglycemia difference

Outcome	*Placebo (n=2333)*	*Empagliflozin (n=4687)*	*Hazard Ratio (95% CI)*	*P value*
1°: Death from CV causes, nonfatal MI, or nonfatal stroke	**282 (12.1%)**	**490 (10.5%)**	**0.86 (0.74-0.99)**	**Noninferiority: <0.001 Superiority: 0.04**
-Death: CV causes	**137 (5.9%)**	**172 (3.7%)**	**0.62 (0.49-0.77)**	**<0.001**
-Nonfatal MI	121 (5.2%)	213 (4.5%)	0.87 (0.70-1.09)	0.22
-*Nonfatal stroke	60 (2.6%)	150 (3.2%)	1.24 (0.92-1.67)	0.16
2°: Death from CV causes, nonfatal MI, nonfatal stroke, or hospitalization for unstable angina	333 (14.3%)	599 (12.8%)	0.89 (0.78-1.01)	Noninferiority: <0.001 **Superiority: 0.08**
-Hospitalization for unstable angina	66 (2.8%)	133 (2.8%)	0.99 (0.74-1.34)	0.97
Death: any cause	**194 (8.3%)**	**269 (5.7%)**	**0.68 (0.57-0.82)**	**<0.001**
Heart failure hospitalizations	**95 (4.1%)**	**126 (2.7%)**	**0.65 (0.5-0.85)**	**0.002**
*Silent MI	15 (1.2%)	38 (1.6%)	1.28 (0.7-2.33)	0.42
*Fatal or nonfatal stroke	69 (3.0%)	164 (3.5%)	1.18 (0.89-1.56)	0.26
*Nonfatal stroke	60 (2.6%)	150 (3.2%)	1.24 (0.92-1.67)	0.16

*denotes non-significant increase in outcome compared to placebo
-denotes element of composite endpoint

All-cause death NNT (~3 years) = 39 patients
CV death NNT (~3 years) = 46 patients

Strengths

- Large, well-designed 1:1:1 RCT at hundreds of sites
- Extremely homogenous baseline characteristics amongst treatment arms
- Statistical analysis of inferiority and superiority
- Evaluation of multiple independent outcomes besides composite endpoints

Limitations

- Mortality/morbidity compared to placebo instead of predetermined standard of care
- No comparisons of background glucose-lowering agents besides insulin
- Possibly limited external validity
    - o questionable extrapolation to patients with uncontrolled CV risk factors
    - o results limited to secondary CV disease prevention
- Data analyzed by study sponsor Boehringer Ingelheim; co-funded by Eli Lilly

Author's Conclusions

Type 2 diabetics at a high risk for cardiovascular disease had a lower risk of death and the primary composite cardiovascular outcome while treated adjunctively with empagliflozin as compared to standard care.

Discussion

The EMPA-REG OUTCOME study provides powerful and exciting evidence that empagliflozin significantly reduces all-cause and cardiovascular mortality in diabetic patients with relatively well-controlled cardiovascular disease. The study suggests especially marked benefit in patients with heart failure, due to the noteworthy and significant reduction in heart failure hospitalizations. In addition, the empagliflozin treatment group experienced significantly lower rates of AKI and acute renal failure, and may reflect a possible element of renal protection in these patients. Commonly concerning adverse effects of SGLT2 inhibitors, such as UTIs and DKA, were not reported more than placebo, despite increased rates of genital infections. The increased rates of stroke and myocardial infarction in the empagliflozin pool were not statistically significant, but they are concerning, counterintuitive to the mortality benefit, and warrant further investigation. Overall, the study's remarkable results may be extrapolated to patients fitting the inclusion criteria, but ultimately more research is necessary to evaluate these benefits in other patients.

Future Studies

- Morbidity/mortality comparison to other glucose-lowering agents with CV or mortality benefit (i.e. metformin)
- Evaluation in patients with poorer disease state control
- Specific impact in heart failure patients
- Cost-benefit analysis and dose-response relationship
- Investigation of mechanism for MI/stroke disparity and long-term effects

SDSHP Calendar of Events

2016 SDSHP Annual Meeting
April 8th-9th
Rushmore Plaza Holiday Inn, Rapid City, SD
To register: http://www.sdshp.com/event/2016-sdshp-annual-meeting/
The schedule: http://www.sdshp.com/2016-sdshp-tentative-schedule/

To help promote the Practice Advancement Initiative in South Dakota, the SDSHP Annual Meeting, held on April 8-9th in Rapid City, will include 2 hours of CE focusing on practice advancement. ASHP Vice President of Practice Advancement, Doug Scheckelhoff will be speaking on rural practice advancement on April 9th. Following his presentation, we will be having one hour of practice advancement pearls and lessons learned in SD. Please join us at this year's meeting for continuing education credits, networking, and fun!

ASHP House of Delegates

The ASHP House of Delegates is responsible for the Society's stance on important issues related to health-system pharmacy practice and medication use in society. The House of Delegates meets annually at the ASHP Summer Meeting and has a virtual House of Delegate session in March and November.
Please use the following link to review the policies that will be voted on during the March Virtual House of Delegates. The policies are attached under the Agenda and Action Items section.
http://www.ashp.org/DocLibrary/Policy/HOD/HOD_Agenda.aspx

If you have any questions/concerns relating to these policies please forward your questions to the SDSHP representatives for this year.
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Spotlight

Do you know of any pharmacist that should be spotlighted in this newsletter based on how they are advancing pharmacy practice? If so, email sdshp at: sdshp.sd@gmail.com and they may be highlighted in an upcoming edition!