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Chronic kidney disease due to diabetes is a worldwide problem. It occurs across all races and as of 2014, there were approximately 159 new cases per one million people in the United States, which translates to more than fifty-one thousand new cases across the U.S. per year [1]. As reported by the CDC, 9.3% of the population has diabetes[2]. According to statistics published by the American Kidney Fund, diabetes is the number one cause of chronic kidney disease (CKD), accounting for 44% of all new cases [3].

Chronic kidney disease is treatable and with early diagnosis, it is possible to slow its progression[4]. However, if the disease is not detected and treated early on, the result is the need for a transplant or dialysis. In the United States, 6.7% of the Medicare budget is spent on dialysis, this significant expense applies to only 1% of the covered population [4].

In the pilot study done by the Kidney Early Evaluation Program (KEEP), researchers aimed to "determine the feasibility of identifying individuals at increased risk of CKD and to promote public and patient education" [5]. The study provided free-community based screening in 21 cities nationwide based on individual increased risk of CKD. Anyone over the age of 18 with a personal or family history of diabetes or hypertension, or a family history of CKD were screened. The study found that only 6.7% of the participants were aware of their diagnosis of CKD, yet 28.7% of participants met the diagnostic criteria [5].

The target audience for my presentation is adults over the age of 18 with Type 1 or Type 2 diabetes living in Coos County Oregon. While the national rate of diabetes is 9.3%, the rate of diabetes in Coos County is 10.9%[6]. In 2011, diabetes was the 7th leading cause of death in Oregon and the death rate due to diabetes has steadily increased since 1990 and is higher than the

US rate [7]. That same year, the cost of diabetes related hospitalizations in Oregon reached more than 91 million dollars[7].

As previously stated, diabetes in the number one cause of CKD. In fact, 40% of people with diabetes mellitus, regardless of which type, will get CKD [3]. As a means of determining ways to prevent or slow the progression of CKD, the ADVANCE trial looked at tight glucose control and its effect on kidney health. The trial split participants into two groups, one with an intensive glucose control goal of an A1C of 6.5% or less, and one with a standard A1C goal [8]. The study followed diabetic patients for a median of 5 years and found that the tightly controlled glucose group (average A1C for the group was 6.5% and 7.3% in the standard group) had a 65% lower risk of developing ESRD, 9% of microalbuminuria, and 30% of macroalbuminuria [8]. It was also evidenced that tight control reduced the progression of albuminuria by 10% and increased the regression by 15% [8]. As a result of studies similar to the ADVANCE trial, intensive glucose control as a way to slow or prevent CKD is a method that has become standard of care across most large organizations, including the Joslin Diabetes Center, The National Institute of Diabetes and Digestive and Kidney Diseases, and the American Diabetes Association [9-11]. That being said, it is recommended for patients to discuss A1C goals with their providers prior to working towards them, as lower results are associated with increased episodes of hypoglycemia. Specifically, extra caution should be used in elderly patients, those with impaired hypoglycemia awareness, and patients with multiple comorbidities.

According to statistics published by the American Kidney Fund, hypertension is the second leading cause of CKD, accounting for 28.4% of all new cases [3]. Thus, controlling blood pressure is also regarded as standard of care to prevent CKD amongst most major organizations. While some sources identify ACE-inhibitors and angiotensin II receptor blockers (ARBs) as

superior to other anti-hypertensives in terms of preventing or slowing kidney damage [9-12] other sources claim equality between all classes and simply identify controlling blood pressure as a method of kidney protection. The American Diabetes Association, Joslin Diabetes center, National Institute of Diabetes and Digestive and Kidney Diseases, and CMDT all identify ACE-inhibitors and ARBs as superior to other medications in terms of renal outcomes, particularly ACE-inhibitors, with each resource citing randomized controlled trials (RCTs) as their resources for recommendations [9-12]. However, some studies suggest that blood pressure control in general, regardless of the medication class, is renal protective. A systematic review and meta-analysis of RCTs looking at ACE-I and ARBs vs other anti-hypertensives agents in people with diabetes was published in the British Medical Journal in 2016. The meta-analysis reviewed RTCs looking at outcomes including death, cardiovascular death, myocardial infarction, angina, stroke, heart failure, revascularization, and end stage renal disease[13]. Although early studies showed superiority of ACE-I and ARBs, the results of this study, which looked at over 95,000 patient follow-up years, failed to show a superior class of anti-hypertensives in terms of kidney outcomes [13]. Therefore, the recommendation formed by this meta-analysis is simply good blood pressure control, regardless of drug class [13].

Also of great importance is the Joint National Committee (JNC), which is put together by the National Heart Lung and Blood Institute (NHLBI) in order to create evidenced based treatment guidelines for hypertension based on the data from many randomized controlled trials. According to the JNC 8, *nonblack* adults age 18 and older with diabetes and *no* evidence of CKD should be treated with a thiazide, ACEI, ARB, or calcium channel blocker (CCB), alone or in combination, to a blood pressure goal of <140/90 [14]. *Black* adults age 18 and older with diabetes and *no* evidence of CKD should be treated with a thiazide or CCB, alone or in combination, to a

blood pressure goal of <140/90. In addition, the JNC 8 suggests that adults age 18 and older with CKD *with or without diabetes,* regardless of race, should be treated with an ACE-I or an ARB alone or in combination with another class, to a blood pressure goal of <140/90 [14]. In short, if there is already evidence of CKD, treatment with an ACE-I or an ARB is recommended. However, in regards to diabetic patients *without* CKD, the choice of drug class depends on their race.

In addition to tight glucose and blood pressure control, a third method to protect renal function is regular screenings for all diabetic patients. As previously stated, a study conducted by KEEP involving patients with known diabetes revealed that only 6.7% of the participants were aware of their diagnosis of CKD, yet 28.7% of participants met the diagnostic criteria [5]. One can assume that to identify an occult disease, a patient must be screened for it. Therefore, it can be inferred that not everyone at risk of developing CKD is being screened for the disease. In fact, the ADD-CKD study, which looked at patients with Type 2 DM, revealed that only 12.1% of participants with kidney disease were identified correctly as such by their providers, yet 54.1% had Stage 1-5 CKD based on albuminuria and estimated GFR [15]. The study also revealed that urine protein, urine ACR, and estimated GFR were not performed in 51.4%, 52.9% and 15.2% of patients, respectively [15]. Relatively speaking, clinicians were more astute at identifying Stage 3-5 CKD than Stage 1-2 [15]. Unfortunately, the best time to identify CKD in terms of preventing progression is in the early stages.

A study published by the NIH in 2013 specifically looked at obesity as a risk factor for developing CKD. Obesity results in visceral adiposity, which promotes a low grade inflammatory state and causes the release of macrophages into the kidneys [16]. Consequently, this results in many pro-inflammatory mediators, which are damaging to the glomeruli of the kidney

[16]. Another factor causing damage to the kidney, visceral adiposity produces and releases unique cytokines into the blood [16]. Thirdly, visceral adiposity causes an increase in the activity of the renin-angiotensin-aldosterone system (RAAS), which in turn causes arterial hypertension, adding to kidney injury [16]. Kidney compression, caused by an increase in visceral fat, results in increased tubular reabsorption of sodium chloride, causing volume expansion and therefore arterial hypertension, leading to additional nephropathy [16]. Based on this information, the Joslin Diabetes Center, National Institute of Diabetes and Digestive and Kidney Diseases, and American Diabetes Association all cite weight loss as an important strategy for risk reduction [10,17,18]. In addition, heart health influences kidney health, so any cardiovascular risk reduction will help prevent CKD. Thus, smoking cessation and decreasing lipid levels are both crucial to preserving kidney function [9,10,18].

In order to live their best lives, patients should have a greater understanding of how to prevent end organ damage due to diabetes and be motivated to take an active role in their care. Knowledge is power and knowing how to keep their kidneys healthy is the first step.

The two most important things patients can do to protect their kidneys is to tightly manage their blood glucose and control their blood pressure [19]. They should also talk with their primary care provider or endocrinologist about regularly screening them for CKD. Losing weight is also an important way to protect their kidneys. Lastly, patients should understand that heart health influences kidney health. Therefore, anything they can do to lower their cardiovascular risk will have a secondary positive effect on their kidneys. This includes taking a high dose statin and smoking cessation if applicable.

While the Healthy People program first introduced the goal to, "reduce new cases of chronic kidney disease and its complications, disability, death, and economic costs" in 2010,

they greatly expanded on that goal in the 2020 version [20]. The CDC recognized the growing burden, both financially and health wise, and took aim to push for bigger changes. The 2020 report expanded to include 14 CKD related goals, six of which are further broken down into additionally specific goals [1]. For my efforts, I chose to focus on CKD-9, to reduce kidney failure due to diabetes by 10% [1]. It's an ambitious goal and one I would like to contribute to.

I chose this topic for many reasons. The rate of diabetes in this country is staggering and if not treated probably, it can have many devastating effects on the body. It's the number one cause of CKD, which not only costs our government astonishing amounts of money each year, but it can also greatly reduce a person's quality of life. Most patients with End Stage Renal Disease (ESRD) end up on dialysis as a way to sustain life. The treatment is all consuming and greatly effects a person's day to day life. The patients fortunate enough to get a transplant undergo a dangerous surgery and then take a multitude of drugs to keep their new kidney healthy. These drugs have numerous side effects and suppress their entire immune system, in turn making them susceptible to devastating infections. To be able to educate patients on ways to prevent CKD would be greatly fulfilling to me.

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