Moderator: Thank you. Next, we have Anna Rubinsky with the San Francisco VA Healthcare System and University of California San Francisco, and she’ll be presenting on the implementation of a pilot randomized pragmatic trial of a screening program for chronic kidney disease among non-diabetic hypertensive veterans.

Anna: Thank you. So, my objective today is to describe our recent implementation of a pilot, cluster randomized pragmatic trial that’s using the VA electronic health record to identify participants, deliver interventions and ascertain outcomes. I won’t be presenting the outcomes today, which are in progress.

So, ultimately, the goal of this trial is to evaluate the feasibility and preliminary effectiveness of a screening program to improve care for chronic kidney disease among high-risk patients seen in primary care at the San Francisco VA.

So, chronic kidney disease or CKD is defined as an estimated glomerular filtration rate, or EGFR less than 60 or an albumin-to-creatinine ratio of 30 or more based on readily available blood and urine tests. EGFR can be based on creatinine or cystatin C [PH]. Creatinine is ordered routinely, but cystatin C can improve the accuracy of detection of CKD in some sub-groups.

CKD is associated with increased cardiovascular events, hospitalization, cognitive and functional decline, progression to end-stage renal disease and premature death. CKD affects over 20 million adults in the U.S., is largely asymptomatic and so often is, remains undetected until it has advanced. And, therefore, the majority of patients with CKD are unaware that they have the disease as are their providers.

So, despite high prevalence, high burden of complications, low recognition and easy detection, it’s uncertain where population-based screening for CKD can improve care. This is due to a lack of evidence, and in fact, the U.S. preventative services task force has recently graded the effectiveness of screening for CKD as I, insufficient evidence to make a recommendation.

So, in this trial, we used a VA EHR to identify the potential eligible study sample of non-diabetic, hypertensive veterans with a primary care visit to the San Francisco VA in the past three years and no diagnosis of CKD. Written consent was obtained with providers and patients were mailed information letters and could opt out within 30 days by mail or phone. The study period for the intervention was about a year, from February 2016 to March 2017.

Patients were randomized in clusters defined by their primary care provider team to three study arms, usual care and two incrementally intensified treatment strategies implemented by providers. The first intervention arm included screening for CKD followed by education on CKD management for the providers and the patients. And, then the second intervention arm added co-management of CKD by a clinical pharmacist.

So, for the screen educate arm, patients with upcoming outpatient appointments were identified by EHR data queries that were conducted approximately weekly. And, then triple marker CKD screenings, specifically creatinine, cystatin C and albuminuria laboratory tests were ordered by study staff prior to the upcoming appointment.

The patient’s test results and a positive for CKD, the CKD stage and the corresponding treatment guidelines were then sent by study staff to the primary care provider via and electronic note in the EHR, which would look like this. And, then the patient’s test results were also mailed to the patient along with educational material.

For the screen educate plus pharmacist co-management arm, there was an additional option included in the electronic note for the primary care provider to refer patients who had CKD to a clinical pharmacist for co-management. Upon receipt of a referral, the pharmacist would schedule a series of appointment and education on CKD, blood pressure management and appropriate medication use.

So, 2,293 patients had a prior primary care appointment at the San Francisco VA and met the EHR inclusion criteria. After additional exclusions by the primary care providers and by chart review, study information, letters were mailed to 2,012 patients. Within the 30-day opt-out period, 133 patients opted out by phone or mail and 60 letters were returned undeliverable. So, therefore, 1,819 patients were included in the trial and randomized by their primary care provider to one of the three study arms.

Among patients randomized to the implementation arms, 10% did not have an outpatient encounter during the study period and so did not receive the intervention. Unfortunately, another 44% had an outpatient encounter that was not identified using our approach of querying the corporate data warehouses appointment data approximately weekly. And, next on our to-do list is figuring out if there was some sort of error in the query or if this is a limitation to the way appointments are scheduled or the way the appointment data is captured.

For all patients who were identified as having an upcoming appointment, the CKD screening tests were ordered. And, among these patients, 70% actually went to the lab and completed the testing. 73 new cases of CKD were identified for a screening yield of 20% among those tested.

So, overall, we were able to successfully implement an EHR-based pragmatic trial of CKD screening. We were able to use the EHR to identify high-risk patients to deliver the intervention and ascertain outcomes. We had high rates of participation by providers and patients, and most providers reported no increased burden due to the study in a survey that we conducted. We had higher than expected rates of complete CKD testing among patients for whom the tests were ordered. And, we had high rates of previously undetected CKD among those tested. And, finally, no adverse events were reported by patients or providers.

But, we also had several lessons learned. CKD screening was ordered for fewer than half of the intervention patients. To increase the reach of the intervention, future trials should consider enrolling patients on a rolling basis as eligible patients are identified as having a scheduled appointment with their primary care provider. Alternatively, the screening orders could be bulk ordered for all intervention patients at the study start. For this pilot trial, these approaches were not feasible, because of limited resources and a need to obtain an informed consent via a mass mailing with a subsequent opt-out period. We also recommend that study teams include multi-disciplinary expertise, including an experience VA data expert, as well as clinicians who can validate the EHR data.

We also had significant provider turnover during the study period, which means that patients could’ve switched study arms due to a reassignment to a new primary care provider. So, we had two attending primary care providers leave the practice and 14 residents graduate, potentially affecting 345 patients who would’ve been assigned to a new primary care provider. Therefore, larger future studies should consider randomizing by clinic rather than provider to reduce contamination between study arms.

In this study, our secondary as treated a priori planned analyses will be particularly information with regard to the potential effectiveness of the interventions.

We also learned that frequent face-to-face communication between the PI and the primary care providers and the clinical pharmacists, especially in the planning phase facilitated high rates of participation and engagement. This sort of communication also ensured that the protocol could be designed to follow the primary care and pharmacist workflow and was feasible to implement in these clinics.

So, to summarize, the VA EHR can be utilized to conduct pragmatic trials comparing processes of care. In this study, we used the EHR to facilitate identification of the study sample and delivery of the intervention, and achieved high rates of participation by providers as well as patients. And, we also had high rates of screen detected CKD. So, we hope that some of our real-world lessons from this trial can inform the design of future pragmatic trials in the process of planning a future multi-site trial.

I’d like to thank the key collaborators in this study, including the PI Carmen Peralta, who couldn’t be here today. And, acknowledge our source of funding and NIH R34 planning grant.

Moderator: I think we have time for several questions.

Moderator: And, please go to the mic.

Moderator: Yes.

Steve: Hi, Steve Asch. Great study. I’m really curious about the IRB application for this study. I’m sure I’m not the only person who’s thinking that it would’ve been better if you had not had to do opt-out informed consent. And, yet that’s about the most that we could expect out of an IRB if it were approved as research. Yet, in my mind, screening for chronic kidney disease, it’s standard of care, like the screening itself is standard of care, whatever happens later in the trial. And, so why couldn’t the project have been divided in half where the screening was quality improvement, and then you wouldn’t need an opt-out at all? And, then the later trial, perhaps, be considered research? It would be innovative, but do you think that your IRB would’ve—were you involved in the IRB application at all?

Anna: I wasn’t.

Steve: Okay.

Anna: So, I think…

Steve: \_\_\_\_\_ [00:10:31]…

Anna: …\_\_\_\_\_ [00:10:32] I think a lot of lessons were learned and I think that that is, I think that, I think in an incredibly low-risk study like this, it does seem possible. I, I know that, that the PI did try, but I don’t think that she was aware of the distinction between research and quality improvement, and wasn’t, didn’t try to go through that route. And, it has been suggested to her. I, so I, so the PI of this study is UCSF Nephrologist This was her first VA study, her first foray into VA data. And, I got brought on towards the end, because of my experience with VA data. So, I was not involved in any of the implementation of this, but I am now figuring out sort of some things that went wrong. But, it, but there were a lot of successes and it’s pretty amazing that she was able to, you know, do a first study and implement an intervention like this using the VA, the VA’s EHR. And, that is, for a future multi-site trial, we would like to what you said and hopefully get a waiver of informed consent, probably through UI, the process as you suggested.

Steve: I thank you for your answer, for what turned out to have been an unfair question, although not intended to be.

Carrie: Hi. Carrie Nelson from Seattle VA. I just had a couple of clarifying questions. So, people are excluded at the initial onset with CKD, was that based on an ICD9 diagnosis or a previous creatinine?

Anna: That was based on just an ICD9 code, and then we did do a chart validation among some samples to see how many. So, I mean, there was, as you can imagine, anyone who had, seemed that anyone who had a ICD9 diagnosis of CKD has it, but of course, there are some people in there who have it documented in the notes, but not, not, but based on ICD9 and so that \_\_\_\_\_ [00:12:37]…

Carrie: \_\_\_\_\_ [00:12:38] during the VA and I think there’s a lot of people who probably had a creatinine check whose doctors probably didn’t put CKD on their \_\_\_\_\_ [00:12:45]…

Anna: Well, that’s, creatinine is ordered for lots of people and, and yeah, and…

Carrie: So, that would change…

Anna: …\_\_\_\_\_ [00:12:51]…

Carrie: …\_\_\_\_\_ [00:12:51] right.

Anna: Yes \_\_\_\_\_ [00:12:53]…

Carrie: \_\_\_\_\_ [00:12:53]…

Anna: …yes. Yeah.

Carrie: And, then the other thing is the VA’s really moved toward same-day access for primary care. So, doing your queries weekly, you’re probably going to miss a lot of people, just…

Anna: Yeah, that’s what I think, that’s what I think it is. I mean, I, I looked at, I didn’t write the code, but I looked at it, and the code looks fine to me, and I need to dig into it. But, that is what I think it is, although, except that, I mean, except I didn’t, I was able to look at when it was scheduled, and it seems like most people had at least one appointment that was longer than a week. But, still I think that that weekly query is problematic, because there’s so many changes to appointment and because so many appointments are scheduled in less than that period.

Jonathan: Jonathan Shaw. \_\_\_\_\_ [00:13:39] primary care physician. Actually, my, my question was similar to that, was what percentage of those people actually already had a creatinine in the record that would’ve, you know, you could’ve just relied on that to trigger the intervention, rather than, you know, having to go through all that steps to get them in a for a lab.

Anna: Well, part of it is also that, I mean, that’s true, but we, so this team has done a lot of work on other measures of kidney disease, including cystatin C, which is more accurate in some sub-groups. And, so they definitely wanted a more accurate screening panel. But, but there is certainly existing creatinine on many patients that can be utilized.

Jonathan: Yeah. And, when I saw the cystatin C, I was like, oh, there’s definitely a nephrologist involved. I wonder…

Anna: They are all nephrologists. I’m the only non-nephrologist on the study team.

Jonathan: So, I mean, another thing worth looking at, just in terms of implementation is whether, how much difference that cystatin C measurement made. I mean, if you would’ve gotten say 19% instead of 20% just with your creatinines, or if you would’ve gotten 15% just by looking at labs they had in the past year, you might realize that the real value is in the intervention later and not all the effort in getting those labs, since that was the hard part. So, that’s just a suggestion to look at.

Anna: That’s a great suggestion. We actually haven’t talked about doing that. But, obviously, that’d be really easy to do. And, I mean, I, and I agree, it’s that, it’s, it’s giving the providers the results, so here are the results, here is the stage of their kidney disease, and here are the corresponding treatment guidelines, not, yeah, not the addition of cystatin C \_\_\_\_\_ [00:15:18] probably that has the impact.

[Applause]

[End of audio]