

WEBVTT

NOTE duration:"00:25:03.6610000"

NOTE language:en-us

NOTE Confidence: 0.819005787372589

00:00:00.040 --> 00:00:03.330 Introduction invitation to presents from work today.

NOTE Confidence: 0.90273529291153

00:00:06.930 --> 00:00:11.490 Now these are my disclosures some consulting fees in research support.

NOTE Confidence: 0.897685587406158

00:00:12.960 --> 00:00:44.800 So I don't think it's difficult to get everyone across the finish line here that cancer care is increasingly complex right so we have greater understanding of the molecular genetic background of cancers. We have greater recognition that breast cancer is not 3 things. But many more. We actually recognize more than 100 different blood. Cancers currently in a WHO 2016 and this is not only let it increase diagnostic complexity, but greater understanding the diseases lead to new treatments. So there's been about 50 new cancer therapies approved in the last 5 years.

NOTE Confidence: 0.912416934967041

00:00:44.800 --> 00:01:05.380 And most of these new therapies are novel, either a small molecule inhibitors or immunotherapy's. They really have administration as well as side effect profiles that are dissimilar from our traditional set of toxic chemotherapy really was the main state of medical oncology. For decades combine that with an aging population and we really have a greater complexity and delivering modern cancer care.

NOTE Confidence: 0.884220063686371

00:01:05.980 --> 00:01:35.990 And So what do we know about delivering complex cancer care. In fact if we look at the surgical literature. We understand that the clinical volume is actually important both at the surgical surgeon provider volume as well as hospital if you look at GI malignancies or lung cancer movies. You'll see similar analysis done which show that as the experience of a surgeon goes up hospital experience goes up typically outcomes are better, so this is esophagectomy the next 5 slides will be focusing on.

NOTE Confidence: 0.903249204158783

00:01:35.990 --> 00:01:59.170 On this um level surgery, which is quite complex in hospital mortality rate being about 5 to 10% and there's been a number of observational research studies that have shown but with provider in hospital level volumes associate with outcomes. This is the meta analysis to take away

if you are having esophagectomy to low volume hospital, 8.5% mortality in 30 days compared to 2.8% in high volume hospitals.

NOTE Confidence: 0.899840176105499

00:02:00.560 --> 00:02:28.250 So recognizing this Association is lead different uh nations to different policies so in the UK. They started seeing this data, and they basically centralise esophagectomy starting 2001. We don't have that level of centralization United States. But we do have these volume based selective purchasing and so effectively. The first patient safety organizations that look at volume of the hospitals look at the quality metrics and they guide insurance is to contract with higher volume higher quality hospitals.

NOTE Confidence: 0.887665152549744

00:02:29.820 --> 00:02:49.380 So what's the policy outcome here, so in the UK. If we look back in the last decade, the provider volume. Esophagectomy surgeons doing that, Sausage Ectomy. Their average case, number is 20 per year in the US. That's 4.9. There certainly are large volume providers here, but there's a lot of care being driven by the lower volume hospitals.

NOTE Confidence: 0.897116601467133

00:02:49.960 --> 00:02:59.980 Not the end of the day, the hospital mortality rate for esophagectomy in the US is actually inferior to the UK an on multi variable analysis, the volume is a major driver.

NOTE Confidence: 0.892395317554474

00:03:01.120 --> 00:03:18.510 So it's generally accepted that clinical volume is a social without comes following complex surgeries. The mechanisms likely multifactorial certainly surgical skill was important proficiency, but also process of care hospitalization organization, having specialized units. Having the appropriate nursing to staff ratio.

NOTE Confidence: 0.869258761405945

00:03:19.170 --> 00:03:49.900 While we know surgical importance of clinical volume in and out comes the really has been understudied of the non surgical app location of Volume Outcome Association for complex. Non surgical care is really uncertain. It just has not been studied and so where is cancer care medical oncologix delivery United States. It's primarily in the community setting so about 80% of care is in the community 20% or facilities like here, an academic setting.

NOTE Confidence: 0.886055469512939

00:03:49.900 --> 00:04:22.230 The majority of Oncologist in the general community are generalists. They see of variety of cancers each and every day and our research question was really whether there is Association between the experience of delivering care for specific subtype of cancer and those subsequent clinical outcomes and so we initially focused on my own clinical specialty, which

is lymphoma and we focused on diffuse large B cell in Phoma, which is the most common of the lymphomas its meaning age is about 70 and so our group has access to Medicare claims data and so.

NOTE Confidence: 0.84093302488327

00:04:22.230 --> 00:04:35.720 We typically like to to study diseases out of the aging and it's highly aggressive. It's untreated defuse RGB song. Thermal will lead to mortality within weeks, but it's actually highly curable with him know chemotherapy.

NOTE Confidence: 0.89214015007019

00:04:38.200 --> 00:05:05.560 And so consensus guidelines recommend me to chemotherapy for the few search B Sullivan. Regardless of age. But there are certainly concerns and I think just concerns over treatment toxicity and that actually limits administration in the older population. So I posses going to the study was that patients managed by Oncologist with greater experience by doctors treating older individuals when Phoma would be associated with greater treatment selection and overall survival.

NOTE Confidence: 0.89800226688385

00:05:06.370 --> 00:05:28.060 And so for this analysis, we use here medic air Sierra is a group of cancer registries that come together, including Connecticut, which capture clinical demographic as well. Survival information incident cancers in these regions. We can then link that cancer registry data to comprehensive Medicare claims and effectively you cover about 25% of the entire Medicare population United States.

NOTE Confidence: 0.865120112895966

00:05:29.100 --> 00:05:59.820 And so with that data we conducted a population based cord study of patients greater than 66 years of age that were newly diagnosed with lymphoma over about 10 years. The primary outcomes are analysis for threefold. One was treatment. Selection did a patient that had a new incident case of who starts Beasley Farmer received chemotherapy and if they did was a guideline recommended wasn't anther cycling cured of intent treatment. We then looked at earlier hospitalization rates looking at the 30 day after chemotherapy initiation and then finally overall and with Phone with specific survival.

NOTE Confidence: 0.882528305053711

00:06:00.870 --> 00:06:31.180 So if you look at the surgical literature, most of the volume outcome studies use an aggregate volume and so instead of this kind of more aggregate or average. We try to be a little bit more refined in our volume and So what we did is we actually looked at a number of lymphoma treatment initiations and Medicare claims data provider had within the last 12 months of each incident. DLBCK so it's a rolling volume measure. An we borrowed from

the surgical literature of this idea of doing turpial so we had a low medium and high volume provider characters characterization.

NOTE Confidence: 0.865598618984222

00:06:33.310 --> 00:06:43.420 So, in this analysis, we identified about 8200 Medicare beneficiaries that were newly diagnosed the fuselage pizza lymphoma and they receive their care from about 2500 Oncologist within Sarah Medic care.

NOTE Confidence: 0.880694508552551

00:06:43.930 --> 00:06:58.030 These Oncologist initiated treatment of total about 25,000 Medicare beneficiaries with lymphoma so that's diffuse large B cell in Phoma. Among other histology's in the median number in the last 12 months for these providers was too with a range of zero to 30.

NOTE Confidence: 0.889376521110535

00:06:59.960 --> 00:07:29.720 In here, the outcomes, so about 75% of patients that are newly diagnosed diffusers. Libya song Thomma receive at least a cytotoxic chemotherapy and you had a greater odds of receiving chemotherapy as you went to a higher volume provider so low medium high. This was kind of a dose dependent Association and these are multi level. Logistic regression analysis or have covariates, including things like age sex, race corbetti disability status among others. So pretty robust adjustment in these models.

NOTE Confidence: 0.88836145401001

00:07:30.560 --> 00:07:52.210 So that's receive chemotherapy and those patients that receive chemo was that chemo with curative intent was it. A guideline recommending therapy and you see here that 71% of patients received a guideline recommended regimen and again. It was more likely that you would see a guideline recommended if you saw a provider it with greater experience treating patients in an older adults.

NOTE Confidence: 0.880559623241425

00:07:52.930 --> 00:08:13.380 And then Lastly hospitalization occurred in about 26% of patients that were newly initiated on therapy in the odds for hospitalization were lowest in those patients that were treated by the highest volume providers so at the end of the day hire. Oncologist fine with social with receipt of chemotherapy greater odds of receiving treatment with creative intent and then having lower odds of hospitalization.

NOTE Confidence: 0.895970404148102

00:08:14.460 --> 00:08:35.950 This is our survival analysis and so on unadjusted analysis, you see here there's some separation of the curves with the highest volume providers. Those patients having the greatest survival when we do multivariable. Cox regression analysis. There is about a 15% reduction in the risk of death. If you receive care by the highest tertile of alone what provider.

NOTE Confidence: 0.893342256546021

00:08:37.850 --> 00:09:02.960 If we look at the subgroup of patients at receiving guideline recommended therapy. The Volume Survival Association goes away. And so our thought is that the volume of hospitalization as well as if I'm survival is really in part due to greater selection of the appropriate chemotherapy. A greater understanding of toxicities. Perhaps as well as intensification and so this is what we find here that that volume. I'll come basically goes away.

NOTE Confidence: 0.878152310848236

00:09:04.050 --> 00:09:35.330 So that's diffuse large B cell in Phoma. We next wanted to look at whether via Malcolm Association is persistent looking at a specific treatment so as a provider gets more experienced giving a certain treatment are those outcomes of that treatment better and so for that. We looked at retaks amount. So why look over talks about this is the first approved monoclonal antibody that was approved in 1997. It binds CD 20 on B lymphocytes and in randomized trials. It's approved survival across many B cell subtypes while it's really well tolerated.

NOTE Confidence: 0.892289578914642

00:09:35.330 --> 00:09:59.270 Now there's a unique and also unique side effect of infusion related reaction, which quite common, so patients experience in future interactions during the 1st or 2nd dose if they tolerate the first or second dose. They typically do very well with this treatment in while most reactions are manageable with things like Benadryl and steroids. There are few life threatening events that could perhaps increase the concerns of providers without as much experience.

NOTE Confidence: 0.875348389148712

00:10:00.030 --> 00:10:19.740 And so we use a similar population population based cohort study that use your medic air to assess outcomes in these patients initiating Rituxan. Mab we hypothesize providers with infrequent use of Rituxan. Mab may be less familiar managing the side effects and thereby patient seeing these lower volume providers would be more likely to discontinue treatment receiving just one or 2 doses.

NOTE Confidence: 0.893135130405426

00:10:20.660 --> 00:10:44.340 And so here we have the primary outcome or really discontinuation of this drug defined as less than 3 doses of Rituxan. Mab within 180 days of initiation typically rituximab given for 4:00 to 6:00 doses over the first six months in our primary predictor value was very similar to the previous we had a 12 month look back. But instead of counting lymphoma cases, we counted? How many times provider had initiated Rituxan mab in Medicare.

NOTE Confidence: 0.88120174407959

00:10:44.930 --> 00:10:47.180 Again, we use the low medium high volume.

NOTE Confidence: 0.879368484020233

00:10:48.620 --> 00:11:08.850 And so this wasn't just a few sorsby cinema. This was all B cell non. Hodgkin's lymphoma. So it's a larger population weighted by 18,500 patients and we link them to a very similar group of Oncologist, 2600, almost 2700 providers. We limit our analysis to those that were alive for 180 days so they could be exposed for the 100 days, which was in our outcome.

NOTE Confidence: 0.884180724620819

00:11:10.010 --> 00:11:27.810 So we find 7.6% of patients actually discontinued Rituxan mam, which is higher than that. We see in clinical trials, usually to buy 1 to 3% again. This is an older population. There's certainly competing risk here, but this was a pretty significant increase that we weren't entirely expecting.

NOTE Confidence: 0.885833621025085

00:11:28.870 --> 00:11:56.860 We also find here, the provider level volume or experience, giving their attacks map is associated with risk of early Discontinuation again. This is a dose dependent where we have the highest volume providers. Those patients treated by them are less likely to discontinue treatment and if you go to the lowest volume you have the greatest risk so compared to patients treated by physicians with greater than 3 Rituxan initiations in the last year that was treated by the providers without any or 57% more likely to discontinue rituximab.

NOTE Confidence: 0.870156407356262

00:11:59.590 --> 00:12:27.440 So we next looked at discontinuation survival. So we have randomized data to show that hurt us have improved survival and you have to get Rituxan mab to benefit from it. So those patients had it really discontinuations did did poorly. You can see here is separation of the Kurds in these findings were consistent on both the 12 month landmark analysis as well as the sensitivity analysis where we only looked at dropping the Rituxan mab so patients were on our chemo. They stop the are continuing chemo and in those situations outcomes were again inferior.

NOTE Confidence: 0.88514244556427

00:12:29.280 --> 00:12:55.030 So the summary these 2 studies is really similar to complex healthcare settings of surgery. We find on colleges experience or volume is associated with important outcomes into lymphoma settings. The first being diffuse large B cell lymphoma where we find greater on colleges experience treating older. Adults is associated with receipt of guideline recommended chemo lower hospitalization and automated survival and then in Rituxan. Mab we actually find greater experience using the drug associated with lower risk of treatment discontinuation.

NOTE Confidence: 0.900278329849243

00:12:56.550 --> 00:13:10.290 So how do we improve upon Cranston delivery by addressing this volume relationship her complex surgeries were technical skills and process of care may not be readily transferable. I would argue that perhaps centralization is actually quite important in doing so.

NOTE Confidence: 0.91426956653595

00:13:11.230 --> 00:13:30.750 Not the case for medical oncology in really medicine in general, where I would expect that clinical experience and knowledge is is much more readily transferable. But I would argue that the current approach that we generate and disseminate knowledge? Is is really outdated. We live in a fast pace cloud based world and we should be able to generate and disseminate knowledge better.

NOTE Confidence: 0.894634962081909

00:13:31.270 --> 00:13:57.710 So our post approval world is really data rich and our data poor opinion rich where we have randomized control evidence that really is quite narrow. We have an average affect size. We have a trial population that doesn't represent the general population. We often lack comparative effectiveness. Between 2 suitable treatment options and then many of our day-to-day clinical decisions are not informed by high quality events. These are including things like drug related toxicity management oncology, So what might the path forward.

NOTE Confidence: 0.908753991127014

00:13:58.660 --> 00:14:29.140 So if you read jam in New England Journal every month every month. We see new kind of viewpoints on moving towards a rapid learning healthcare system using big data. This is one such kind of schema where we have a wealth of information's digital knowledge area patient demographic personal clinical data. If you put that in a computer. You have machine learning AI. You're synthesizing finding new associations and then having that go back to the clinician to help make decisions and this is an iterative process.

NOTE Confidence: 0.862916588783264

00:14:30.570 --> 00:15:03.560 So what potential insights from white to big data derived for us in the in our settings that we presented earlier diffuse large B cell. Informer, tux omab. It's likely that higher volume providers reduce the dose of chemotherapy for that first cycle and then escalate treatment. That's fairly nuanced thing that I think high volume providers. Do we might actually derive that from this big data. Similarly, Rituxan mab often will have high dose therapy would split the dose over 2 to 3 days, escalating dose in kind of improving management and tolerance of the therapy.

NOTE Confidence: 0.892693161964417

00:15:03.560 --> 00:15:09.410 So these are the type of insights that we might actually derive from looking at this clinical data.

NOTE Confidence: 0.899977564811707

00:15:10.110 --> 00:15:41.200 Our machine learning does not overcome the inability of observation. Ull data to really produce causal inferences. And so it will be important moving forward to not only have big data but also point of care trials randomization in the clinic embedded within their HR and so for low risk clinical scenarios. I see associations that are identified, using AI in machine learning to be quite sufficient to inform clinical decisions in the support tools. But for most other clinical scenarios. We still benefit from randomized trials. The hope is that we have pragmatic.

NOTE Confidence: 0.875117599964142

00:15:41.200 --> 00:15:55.140 Trials that are really embedded within our smart, THR systems that generate Evanston form a common answer clinical questions. So this is kind of a big picture? What is actually look? How do we go from this to implementation and that's what this pilot study will do so.

NOTE Confidence: 0.871041357517242

00:15:55.790 --> 00:16:26.330 Talk about a brute nib, which is a oral administered tyrosine kinase inhibitor that targets. The root in tires and kindness pathway. It is incredibly effective in CLL. It's a drug that's taken continuously and it's taken until either disease progresses or patients have a major AES in clinical trials drug as well tolerated. It really is quite efficacious. This is the group versus Krampus, ill and you can see here 84% reduction in hazard of progression.

NOTE Confidence: 0.856778800487518

00:16:27.270 --> 00:16:58.440 However, the drug has toxicities and so these taxes are very dissimilar from traditional cytotoxic chemo include things like Arthralgias, which can be difficult to manage GI disturbance bleeding in A-fib. Those are the common that leads Discontinuation and all these toxicities are generally limited in manageable clinical trial rates for discontinuation due to aids were quite low by 5% when you look at the real world, not 40% of patients are discontinuing a brute him due to adverse adverse events, so that's leading to the median duration of therapy.

NOTE Confidence: 0.918639063835144

00:16:58.440 --> 00:17:04.640 Of lesson 18 months compared to clinical trials, where patients are on therapy for 34567 plus years.

NOTE Confidence: 0.899960100650787

00:17:06.630 --> 00:17:40.160 So to try to address this we're partnering with flat iron health flattering health is a real world evidence platform with data and over 2 million cancer patients in United States. Most of this data is really derived from flat irons. Each our system, which is called uncle BHR and that system is effectively used in about 200 comedian called you practices. We've looked at

the data. We have about 5000 patients and flattening that have been prescribed a drug between 2016 and 2019 and the hope is that we can really look at that data to try to identify patterns of care that are associated with improved outcomes and so our hypothesis here.

NOTE Confidence: 0.893636703491211

00:17:40.160 --> 00:17:53.090 Is that patients that are treated by either CL specialist or those providers with greatest experience using a drug will experience loss discontinuation and will be able to find some patterns of supportive care that are associated with experience as well as Discontinuation.

NOTE Confidence: 0.876479923725128

00:17:53.690 --> 00:18:24.560 Ultimately, we aim kind of more broadly to develop and refine approach, that critically evaluates cancer care using large real world data identifies common management strategies for scenarios lacking high quality evidence and then it generates in each are embedded clinical decision tool that disseminates best practices to providers and then if there isn't a best practice. That's available. It actually tests directly these interventions using point of care randomization, so again. What does this look like it's really a hybrid clinical decision support tool and EHR that embedded trial.

NOTE Confidence: 0.707014262676239

00:18:24.560 --> 00:18:25.600 Within 1.

NOTE Confidence: 0.880852818489075

00:18:26.370 --> 00:18:57.060 So this is how we envision it that if a patient or provider rather was going to start a treatment. You would actually get some insight of what other high quality high volume providers are doing and so it says you are initiating a drug name CL specialist with the experience using a drug and obtain routine blood work and see patients frequently during the first three months to identify and managed adverse events would you like to schedule similar follow up to these high volume providers and again, you can say yes you could say no we want certainly physician autonomy, but you would be able to kind of derive? What is the common way that?

NOTE Confidence: 0.870249390602112

00:18:57.060 --> 00:19:00.910 Providers are following their patients and do just that in the community.

NOTE Confidence: 0.89309698343277

00:19:01.550 --> 00:19:19.790 If you have a patient comes in with the toxicity. You would perhaps try to change the dose and there would be prompted to say. Hey why are you ordering this dose reduction? Can we get some information about your symptoms and then the next step really would be to help manage those symptoms. So this patient came in with biologics you select that.

NOTE Confidence: 0.883716285228729

00:19:20.470 --> 00:19:50.560 And the management and a scenario of a mileage is really lacking high quality and so we don't know how best to manage this and so with this approach would do it would look at the railroad data, it would see what are the most common ways that current oncologist or managing this and it would allow randomization to that so in this situation you would basically be able to ask a patient to undergo randomization to the 2 most commonly employed strategies here strategy would be to stop a brute noob and then resume once the symptoms subside and strategy, which is something I commonly do and among.

NOTE Confidence: 0.883252382278442

00:19:50.560 --> 00:20:03.540 Other CL specialist do is we actually initiated Prednisone taper to see if that works again. You could say now a patient could say no but this would allow us to effectively rapidly answer, these questions with high quality data.

NOTE Confidence: 0.882687449455261

00:20:05.410 --> 00:20:19.440 Furthermore, if the patient agreed to randomization this kind of prompt would effectively prescribed the treatment and again. This would actually be informed by the real world data that we're deriving fit in our large datasets.

NOTE Confidence: 0.886308252811432

00:20:20.570 --> 00:20:51.120 So, In conclusion, similar to complex surgical settings provider level volume is a social with important clinical outcomes in older patients with lymphoma. The hope is that by combining big data. Analytics and point of care randomized trials. Rapid learning healthcare systems as well as he's smart HR's will really be able to enable delivery of high quality modern care. How do we do that? We efficiently generate evidence that dresses unanswered questions. We rapidly disseminate. This knowledge back to practicing clinicians and ultimately this will support delivery of complex care in both academics specially practices as well as community oncology.

NOTE Confidence: 0.893527805805206

00:20:52.380 --> 00:21:14.180 So for this, I want to thank you know, copper group as well as some academics deal partners that are working on this. Uh Brewton Project and really this is 4 community based psychologists right so we're trying to derive a tool that would be helpful and so we're really trying to find some community partners to engage with and then finally a flattering as well as the funding for this which was why see pilot as well. the Cal too. I'd be happy to take any questions.

NOTE Confidence: 0.840491533279419

00:21:20.900 --> 00:21:23.440 Yes, we have time for questions.

NOTE Confidence: 0.738272964954376

00:21:26.100 --> 00:21:31.040 Thanks for that position.

NOTE Confidence: 0.823805212974548

00:21:32.080 --> 00:22:02.790 Yeah, so wondering a physicians and have a lot of notifications on their electronic health records are ready like every time they opened it. There's already like a couple of notifications for other meds need to be renewed or like you know follow up appointments and who made so how do you stop them from the nella to these constant popups to like Oh you know would you like to follow like no this recommend of course, because I fell off is already ignored the existing notifications that they get good question so effectively you have to have these process be helpful, so this.

NOTE Confidence: 0.882625639438629

00:22:02.790 --> 00:22:33.360 Development would only occur if we had buying from the community colleges, so this is a tool that would be helpful and perhaps we need to rework and we definitely do need to rework our current EHR to really provide these problems that are helpful that really augment their intelligence when treating patients in a day to day basis, so I don't see our current EHR systems being able to deliver this There's too much noise, but certainly a more refined streamlined EHR, perhaps would.

NOTE Confidence: 0.865534424781799

00:22:33.360 --> 00:22:33.930 In the future.

NOTE Confidence: 0.937473952770233

00:22:36.690 --> 00:22:58.520 Yeah, I guess I along the same lines. One message from all this is that some of these outcomes are not connected to the size of the group, which is a structural issue. That's probably difficult to change across the country or rather an information dissemination and acceptance.

NOTE Confidence: 0.91364324092865

00:22:59.120 --> 00:23:33.600 Yeah, issue and I'm wondering outside of this fairly sophisticated and tech heavy approach is their low hanging fruit in terms of better communication and engagement by the community programs. Yeah, I would argue that smile is one of the best situated groups right so we have academic in care centers that really well integrated much better than many other places in the country so we're doing that in terms of having tumor boards that are inviting community Oncologist to call in so I think this is actually a really.

NOTE Confidence: 0.889932990074158

00:23:33.600 --> 00:23:40.900 Great system to start developing and testing piloting some of these these approaches because.

NOTE Confidence: 0.880317509174347

00:23:41.450 --> 00:24:04.400 I don't think that it's likely that ruling. Cologist will be able to super specialized where I think we're general in colleges will still need to be there, but we're having information tsunami that needs to be parsed and delivered better, so that these oncologist can make the most informed decisions for their patients and I do think tech in kind of smart HR's are probably the way forward.

NOTE Confidence: 0.897794187068939

00:24:05.090 --> 00:24:19.730 And as you mentioned we are bit of an outlier in being a tightly integrated and geographically condensed system. But what about more rural areas places away from academic centers.

NOTE Confidence: 0.879755914211273

00:24:20.760 --> 00:24:48.970 Yeah, so the Aquia Char is used in community centers throughout the country, including including including rural Yale UABU. Penn actually give data so the idea behind that is could we use as big data that includes some high volume specialists and actually disseminate those knowledge that understanding to roll Oncologist in Montana that are using the uncle each are absolutely so that the idea is that we're 1 large community and.

NOTE Confidence: 0.883083760738373

00:24:49.500 --> 00:24:59.260 Yale is relatively small but uncle, which are in flat aren't really sees itself is kind of a national platform and perhaps that maybe the vision of the future.