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Lead-time trajectory of CA19-9 as an anchor marker for pancreatic cancer early detection

Achievement and Impact:

Identification and validation of a robust blood-based biomarker panel indicative of risk of either harboring or developing early stage PDAC



for effective clinical intervention

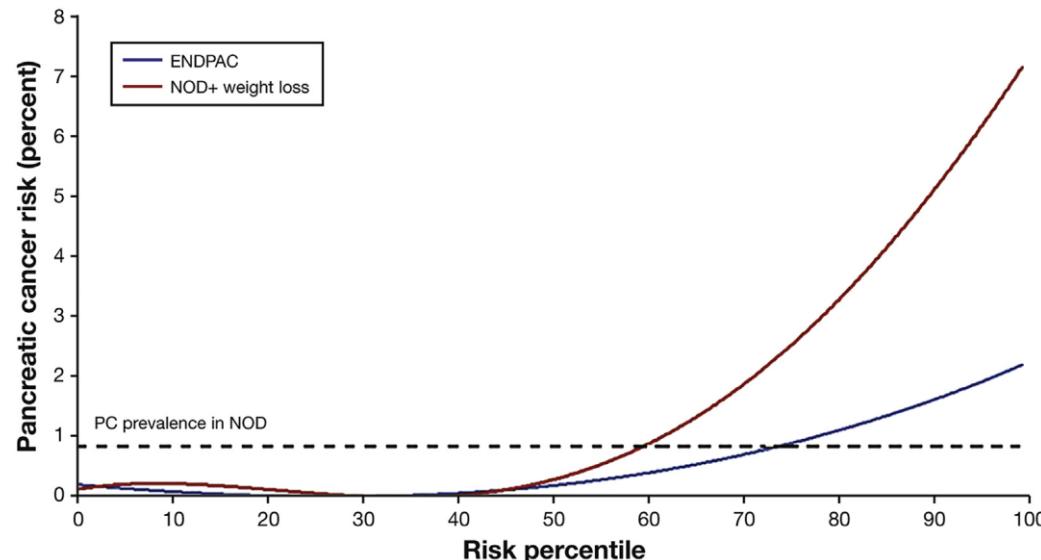


Apply in a high-risk population

New Onset Diabetes and PDAC Risk

6- to 8- fold higher risk relative to general population (Chari ST, *Gastroenterology*)

~1% subjects with new-onset diabetes (NOD) >50 years of age will have pancreatic cancer diagnosed within 3 years following diabetes onset



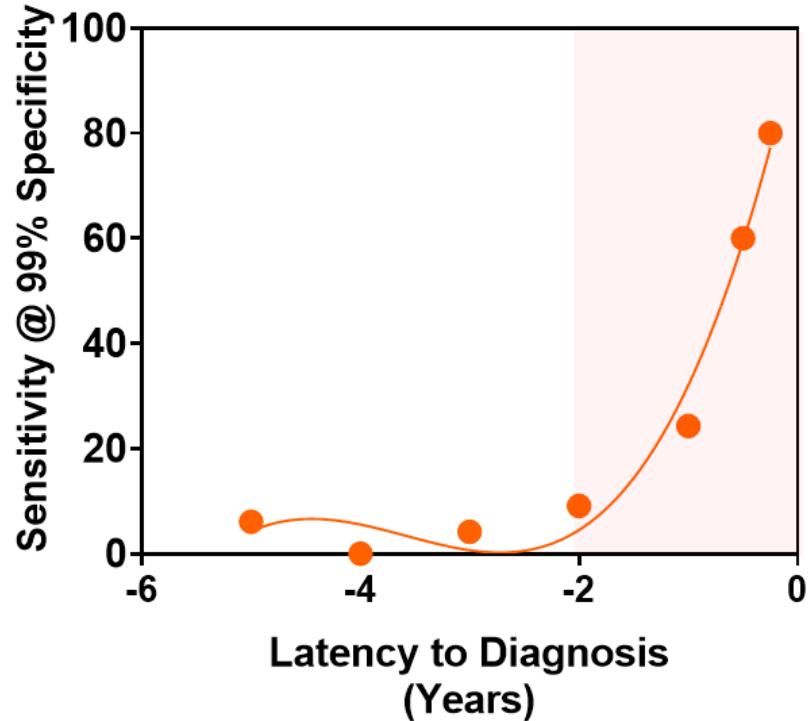
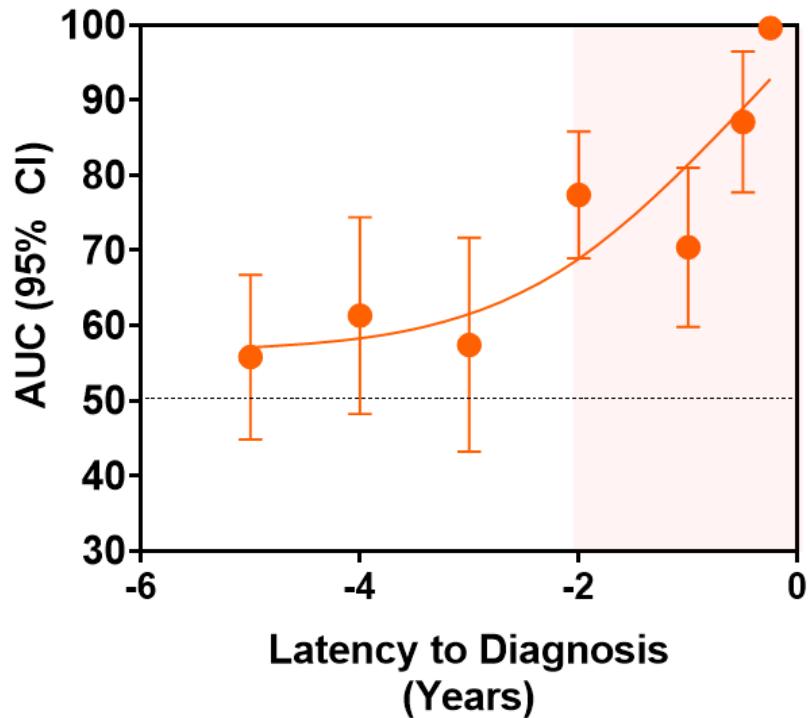
PLCO Cohort

PLCO: 175 PDAC and 875 controls

	# of Years from Diagnosis				
	[0-1)	[1-2)	[2-3)	[3-4)	[4-5)
All Cases	63	32	24	23	33
Localized	13	8	5	2	7
Regional	11	5	7	5	5
Distant	34	19	10	14	15

* Staging unknown for 15 cases

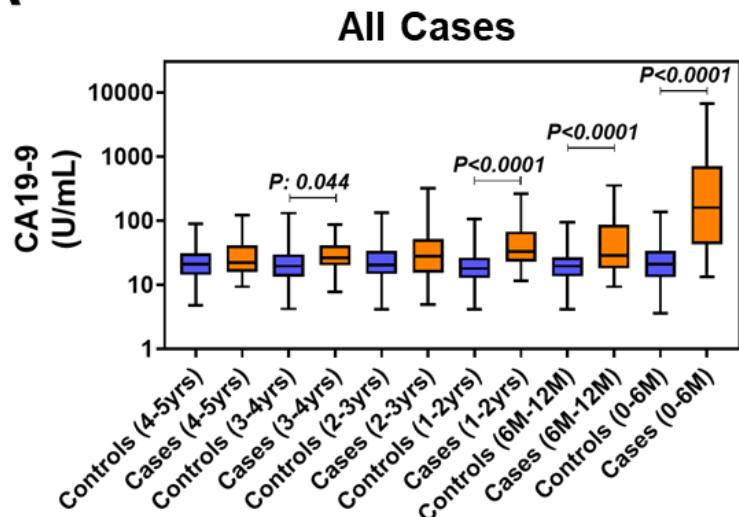
Time-dependent classifier performance of CA19-9 in the PLCO Cohort



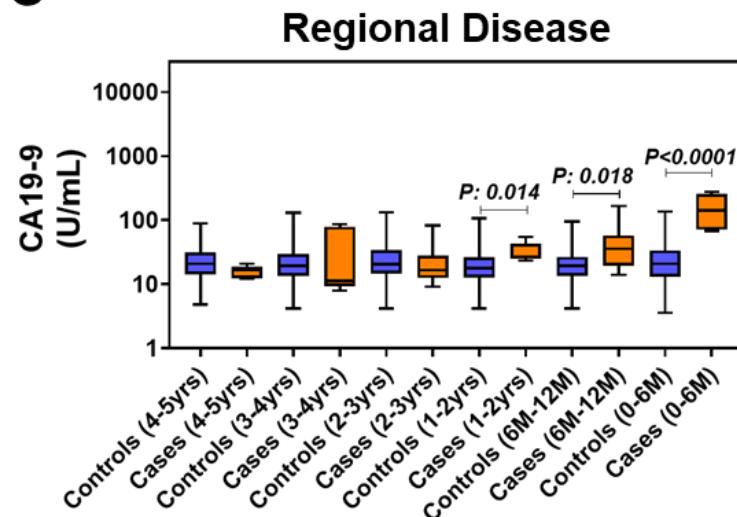
Time to Diagnosis (years)	4+	3-4	2-3	1-2	0.5-1	0-0.5	0-0.25
AUC	0.56	0.61	0.57	0.77	0.70	0.87	1.00
95% CI	0.45-0.67	0.48-0.74	0.43-0.72	0.69-0.86	0.60-0.81	0.78-0.97	0.99-1.000
Sensitivity @99% Spec	0.061	0	0.042	0.091	0.243	0.6	0.8

Distribution plots of CA19-9 at amongst cases and time-interval matched controls various lead-times

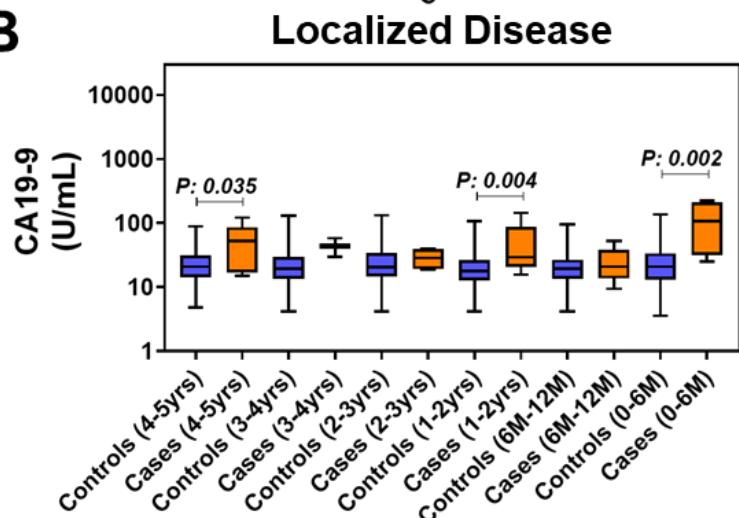
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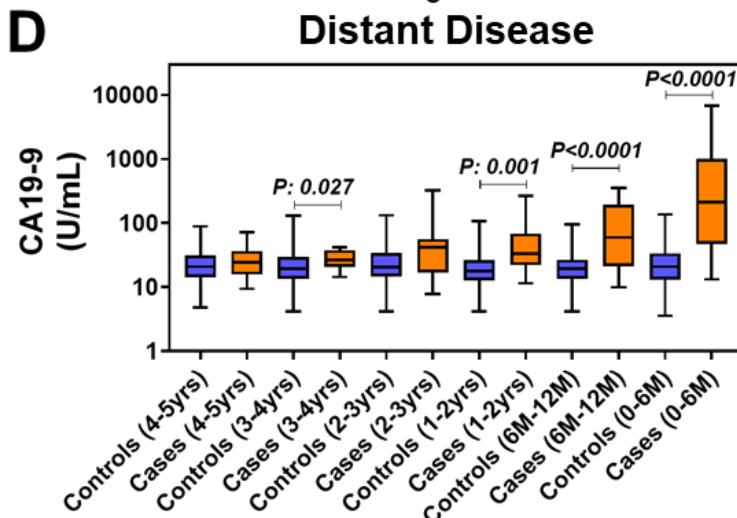
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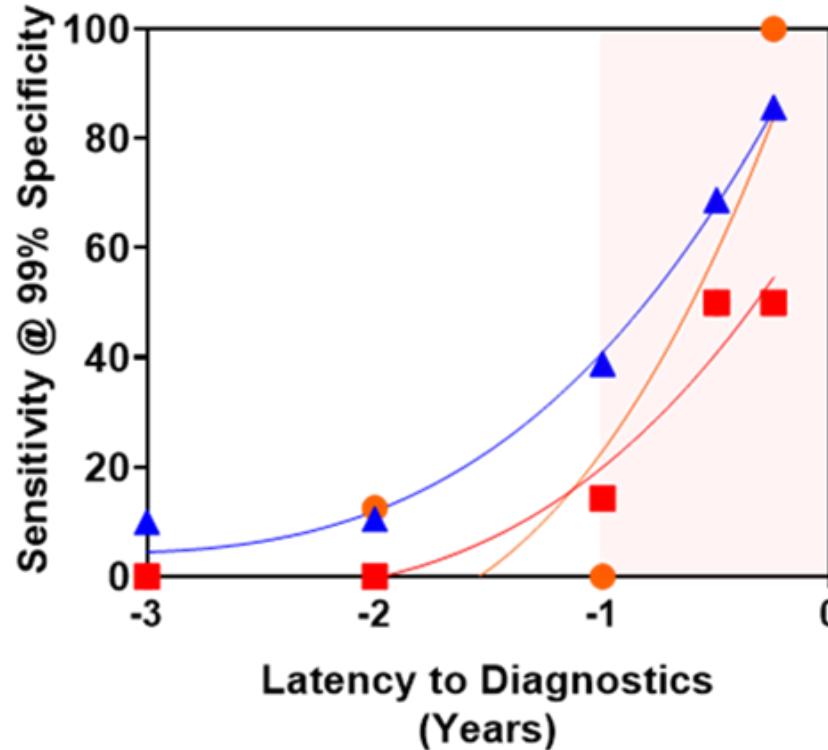
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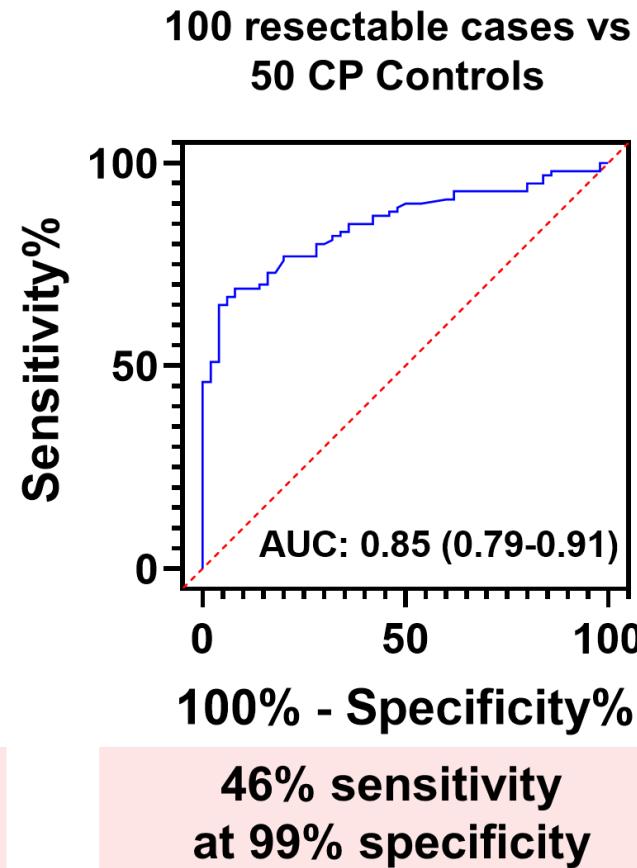
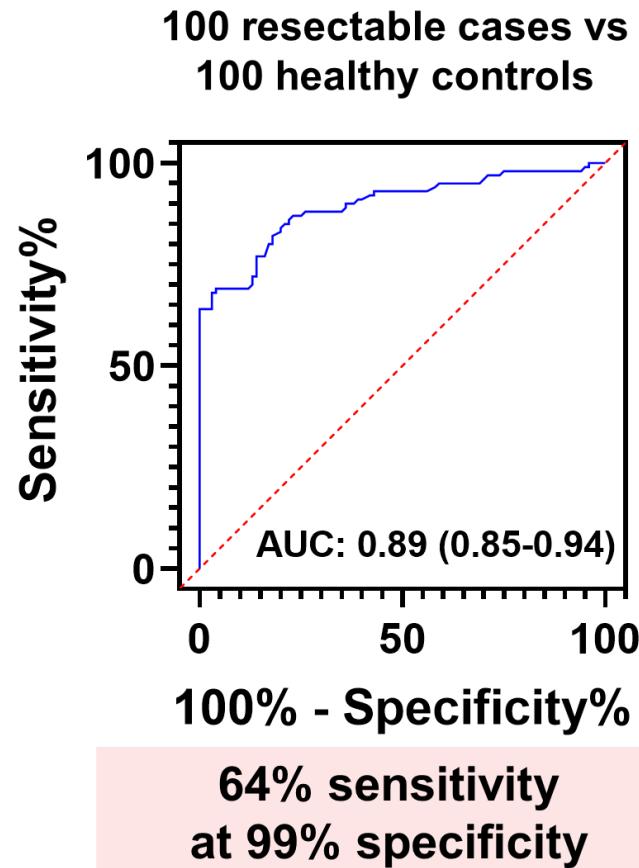
Sensitivity of CA19-9 at 99% specificity for cases stratified based on presentation of localized, regional or distant disease at time of diagnosis in the PLCO Cohort.



■ Localized ■ Regional ■ Distant

~ shift in curve between cases presenting with distant disease versus cases presenting with localized disease is ~6M

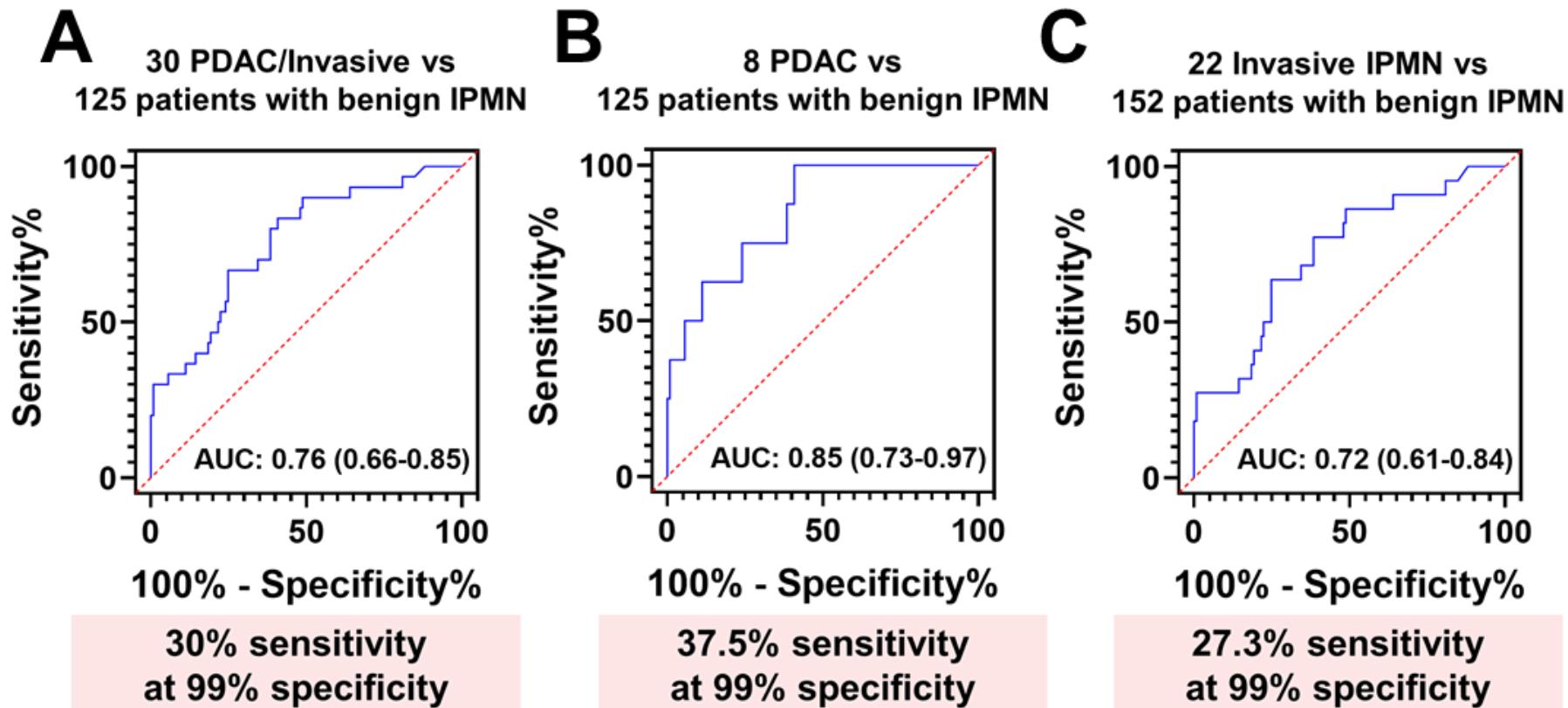
Comparison of CA19-9 classifier performance for detecting resectable pancreatic cancer in the pre-diagnostic and at the time of diagnosis settings



Performance of CA19-9 for detecting of Localized PDAC in PLCO Cohort 6M
prior to diagnosis

AUC: 0.89 (95% CI: 0.74-1.00) with 50% sensitivity at 99% specificity

Classifier performance of CA19-9 for distinguishing malignant cysts from benign cysts



Performance of CA19-9 for detecting of Localized PDAC in PLCO Cohort 6M prior to diagnosis

AUC: 0.89 (95% CI: 0.74-1.00) with 50% sensitivity at 99% specificity

LRG1 and TIMP1 can identify cases diagnosed within 1 year and that were 'negative' for CA19-9 alone based on a 99% specificity cutoff.

PLCO Cohort Within 1 year of diagnosis

		3-marker panel		CA19-9 Only	
		Actual		Actual	
		1 Case	0 Control	1 Case	0 Control
Prediction	1 Case	5	1	0	1
	0 Control	33	306	38	307
		38	307	345	345

McNemar exact test 1-sided p: 0.031

Inclusion of LRG1 and TIMP1 increases sensitivity by 13.2%
1 localized, 1 regional and 3 distant

Conclusions

- CA19-9 offers utility as an anchor marker for screening of pancreatic cancer
- Inclusion of LRG1 and TIMP1 may offer clinical value for identifying cases that do not meet CA19-9 cutoff thresholds

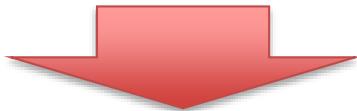


Applied to prospective cohorts of *high-risk* individuals

Moving forward

Primary Objectives:

Develop a blood-based biomarker panel that has utility to assess risk of pancreatic cancer in the context of New Onset Diabetes



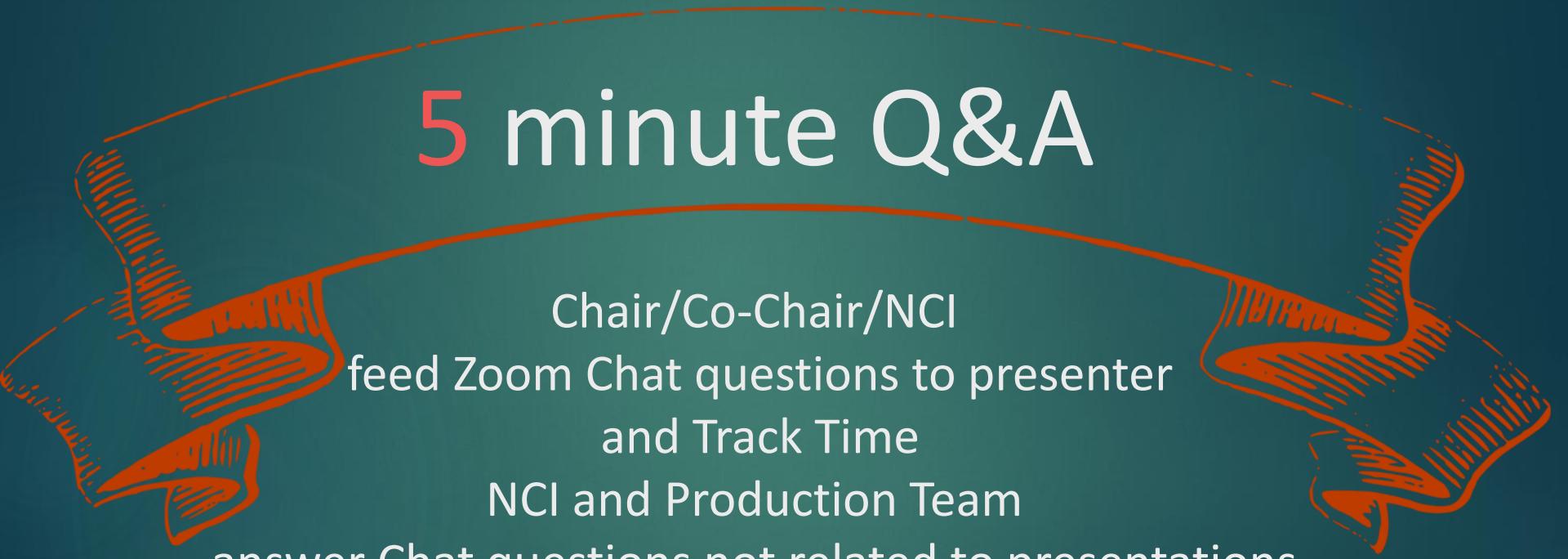
UK Biobank,
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Cohorts

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and Track Time
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answer Chat questions not related to presentations
and use Slack