

Research to Optimize Screening Processes in Diverse Populations

Reissuance Concept Presentation to the NCI Board of Scientific Advisors

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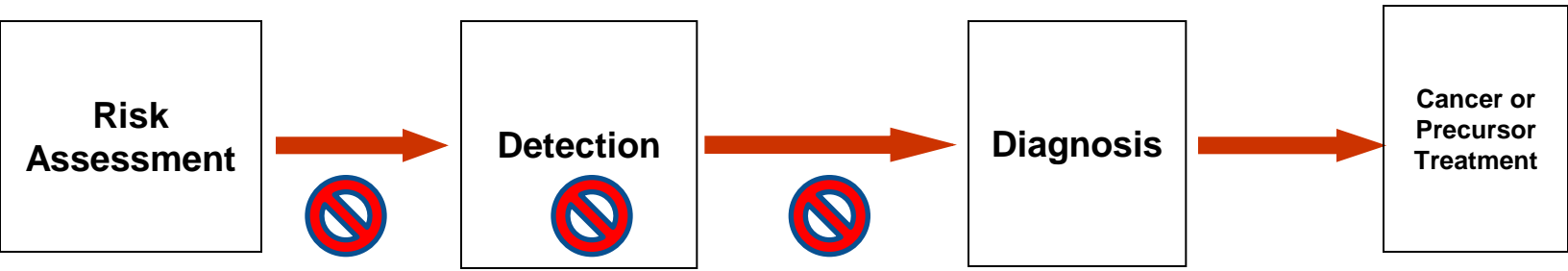
Mortality reductions are possible through screening

- Randomized trial results
 - Breast (mammography) 8 RCTs – 15% ↓↓ mortality¹
 - 40-49 RR death 0.85 (0.75-0.96)
 - 50-74 RR death 0.78 (0.70-0.87)*
 - Colon (I FOBT)** – 13-21% ↓↓ mortality after 18 yrs
 - 4 trials - (RR death 0.85 (0.78-0.92))
 - New tests (FIT) higher sensitivity & specificity
 - Lung (spiral CT)& – 3 trials +, 19% ↓↓ mortality
 - 4 trials – (RR death 0.81 (0.72-0.91))
- Population-based observation (Pap test)
 - Cervix – 20-60% ↓↓ mortality
 - Cervix – 90% ↓↓ Cervix cancer

¹Nelson 2009, *2002 analysis in Nelson et al 2009, ** Whitlock 2008, & Humphrey 2013

Screening is process

And that process breaks down



Patient Adherence

Recruitment Effort
-In reach
-Out reach

Access to Care

Test Sensitivity /specificity

Technical application of the test

Interpretation

Biologic characteristics

Follow-up of Abnormal

Notification System

Patient Adherence

Provider Communication

Diagnostic Evaluation

Sensitivity-specificity

Technical Resources

Interpretation

Tissue sample error

Follow-up of Diagnostic Evaluations

Notification System

Patient Adherence

Provider Communication

Invasive Cx C 56%cx
Late stage Breast 52%brst

32%cx
40% brst

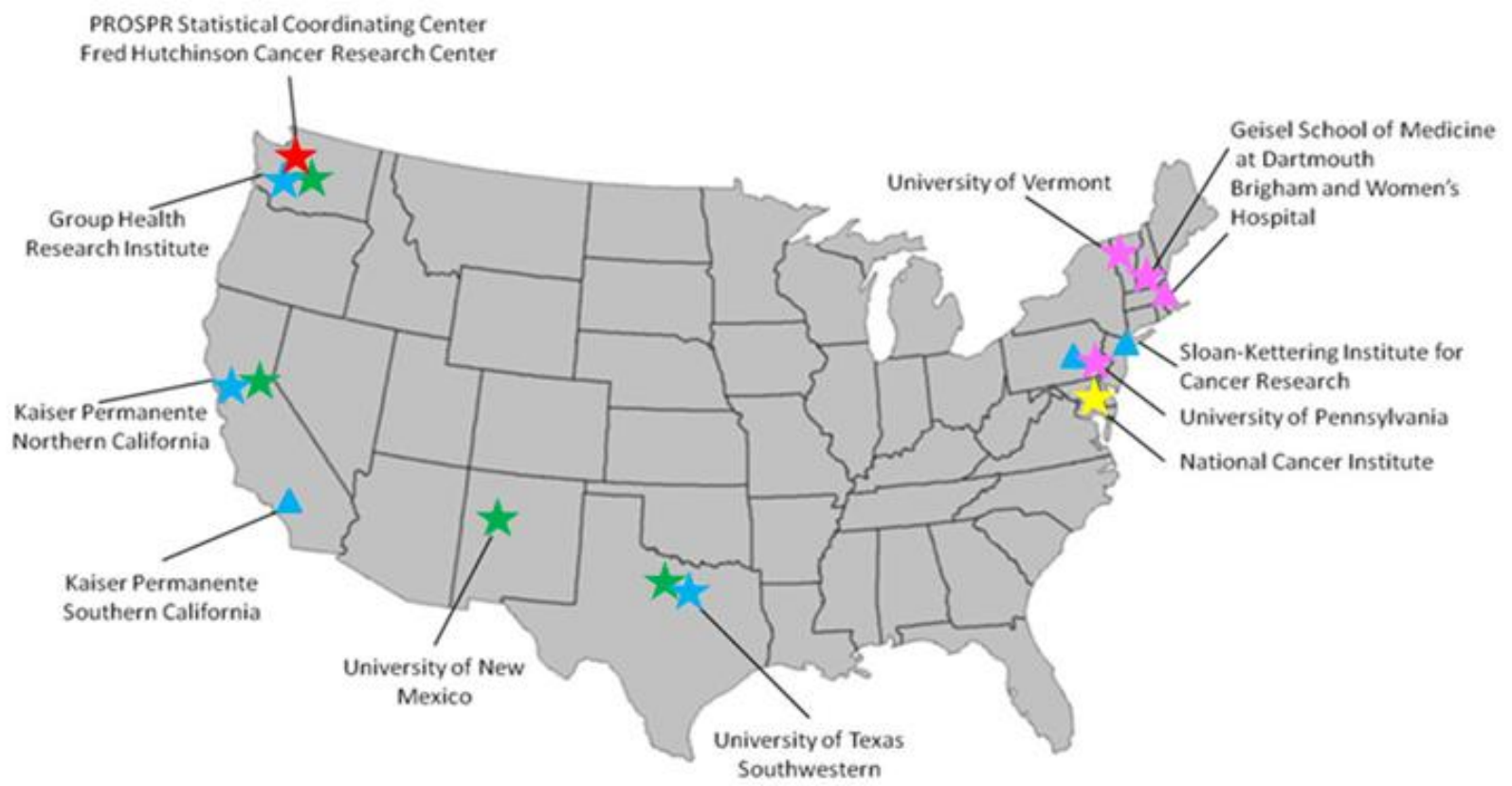
13% cx
8% Brst

PROSPR I – 2011-2016

Document the screening process across 3 cancers

- Breast, Cervical, and Colorectal (CRC)
- 7 centers funded in 2011 (U54)
 - 2 supplements for Cervical cancer 2013
- 1 coordinating center (U01)
- Conduct projects relevant to understanding and improving the process (U54)

PROSPR Research Sites



- ★ Lead Breast Site
- ★ Lead Cervical Site
- ★ Lead Colorectal Site
- ▲ Multiple PI Breast Site
- ▲ Multiple PI Colorectal Site

The centers capture large diverse populations

	Breast Age 18-89 n=309,346	Cervical Age 18-89 n=3,169,645	Colorectal Age 50-89 N=2,381,109	US 2010 Census**
Caucasian race*	74%	50%	59%	79-81%
African- American race*	16%	8%	9%	11-12%
Hispanic ethnicity*	4%	25%	19%	8-14%

* The balance to achieve 100% includes Asian Pacific Islander, Alaska Natives and those reporting multiple races

**Females age 20+ and overall population age 50+

Screening Process Variations Can Have a large Impact

	Breast – 309,346 ♀		Cervical - 3,169,645 ♀		Colorectal – 2,381,109	
Provider /facility	6482 / 221		31,219/2,788		23,110/ 641	
	Lower	Upper	Lower	Upper	Lower	Upper
% abnl	8.6%	10.7%	2.4%	6.3%	4.1%	7.0%
% eval	95%	98%	57%	84%	39%	76%
% Rxed	95%	100%	89%	100%	88%	98%

Breast Cancer has the least variation

$(2.4\%-6.3\%) * 3,169,645 = 123,616$ women

$(76\%-39\%)2,381,109 = 881,010$ people

Organ-based projects – 9 cross-center (35)

Breast – 34 Pubs/13 in progress

- Tomosynthesis vs screen/film – McCarthy et al JNCI 2014
 - Digital breast tomosynthesis (n =15,571) vs digital mammography (n =10,728)
 - Reduced recall (8.8% vs 10.4% p<0.001) – Penn
 - Verified in PROSPR study (8.7% vs 10.4% p<0.0001)

Cervical – 7 Pubs/ 9 in progress

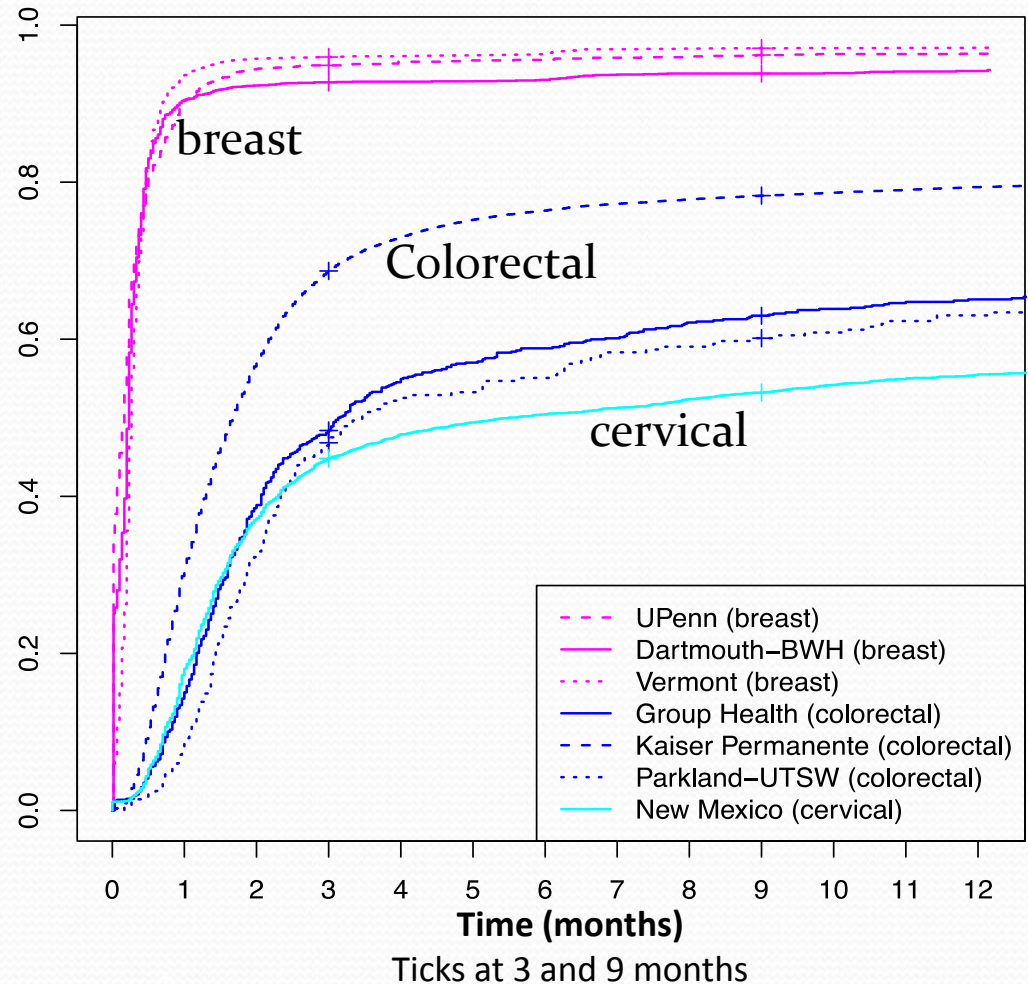
- High-value improvements in US Screening Process ?
 - Kim et al - Annals Int Med 2015 – Disease model
 - Added PROSPR data on frequency of events (abnl, bx, colposcopy)
 - \$15,260/QALY –ve \$19,530/QALY vs no screening
 - ↑ benefit in Quality Adjusted Life years > for adherence to 3 yr & bx

Colorectal - 33 Pubs/ 9 in progress –

- Adenoma Detection rate – NEJM 2014
 - 314,872 colonoscopies by 136 gastroenterologists with 712 interval ca
 - Each 1% ↑ in adenoma detection = 3% ↓ interval ca

Variation in F/u after abnormal screen (abnl) – Tosteson et al

- 7 cross-organ papers published – 14 in process
- JGIM 12/2015
- Time –to F/u after
 - Abnl mammogram
 - Abnl Fit/FOBT
 - Abnl PAP
- Breast – mature
- Colorectal – variation within site (Kaisers)
- Cervical – slowest, now adding site data



What we still need to know

What organizational and provider factors affect the screening process?

- Organizational and provider team variables not recorded in automated records and not standardized
- Comparison across cancers
 - Breast vs. CRC vs. Cervical
- Lung cancer screening
 - False positive evaluation effect

How to measure the quality of the screening process

- Effectiveness, safety, patient-centeredness, timeliness, efficiency, equity

Long-term effects of screening

- Overdiagnosis?
- Adverse events among people who were screened negative

What interventions can improve the screening process?

PROSPR Reissuance

- Greater emphasis on disparities
- Expand data available for screening studies
 - Increase longitudinal follow-up
 - Add Lung cancer screening
- Establish metrics of patient, provider and system factors that affect the screening process
- Evaluate quality of the screening process
 - Effectiveness, safety, patient-centeredness, timeliness, efficiency, equity
- Intervene at some step in the process after screening occurs

Organization & Funding

- Research Centers (U54)
 - 4 research centers (one cancer type per center)
 - At least 2 systems of care (collaborative application)
 - Representation of diverse populations
 - \$12M annual set aside
- Coordinating Center (U01)
 - Data aggregation
 - Annual export of dataset
 - Oversight of quality measurement across cancers
 - \$1.5M annual set aside

Potential impact of PROSPR

After PROSPR, we should have:

- Organizational and provider factors that can be changed to improve screening
- Ways of addressing differential screening across race/ethnicity
- Common measures of quality
- Ways to intervene upon steps in the process
- Ways to measure and achieve improved screening in the United States

Income across PROSPR centers

Table of ZCTA_MedianIncome_calc by PRC within organ group										
Census ZCTA level statistic: Median income	PRC within organ group									Total
	Breast			Colorectal			Cervical			
	Dart/B&W	UPenn	UVT	GHRC	Kaiser	UTSW	GHRC	Kaiser	UTSW	
Census database does not list ZIP	103	86	587	4845	1428	19	4068	1957	70	.
PPT without ZIP	296	1036	793	285	28710	8	346	37946	30	.
Income Q1: <\$51,495	25094 20.3	64378 47.8	45842 40.8	37949 16.7	649831 22.2	48268 72.2	62590 19.2	905752 23.6	132997 74.1	1972701
Income Q2: \$51,495-\$66,465	21970 17.8	22134 16.4	41768 37.1	85794 37.7	710108 24.2	12035 18.0	121473 37.3	944893 24.6	31324 17.5	1991499
Income Q3: \$66,466-\$80,644	25149 20.4	14162 10.5	19599 17.4	56268 24.7	773182 26.4	5198 7.8	78467 24.1	967277 25.2	12691 7.1	1951993
Income Q4: ≥\$80,645	51214 41.5	33888 25.2	5243 4.7	47717 21.0	795649 27.2	1331 2.0	63174 19.4	1015569 26.5	2471 1.4	2016256
Total	123427	134562	112452	227728	2928770	66832	325704	3833491	179483	7932449

Geographic location & PROSPR Centers

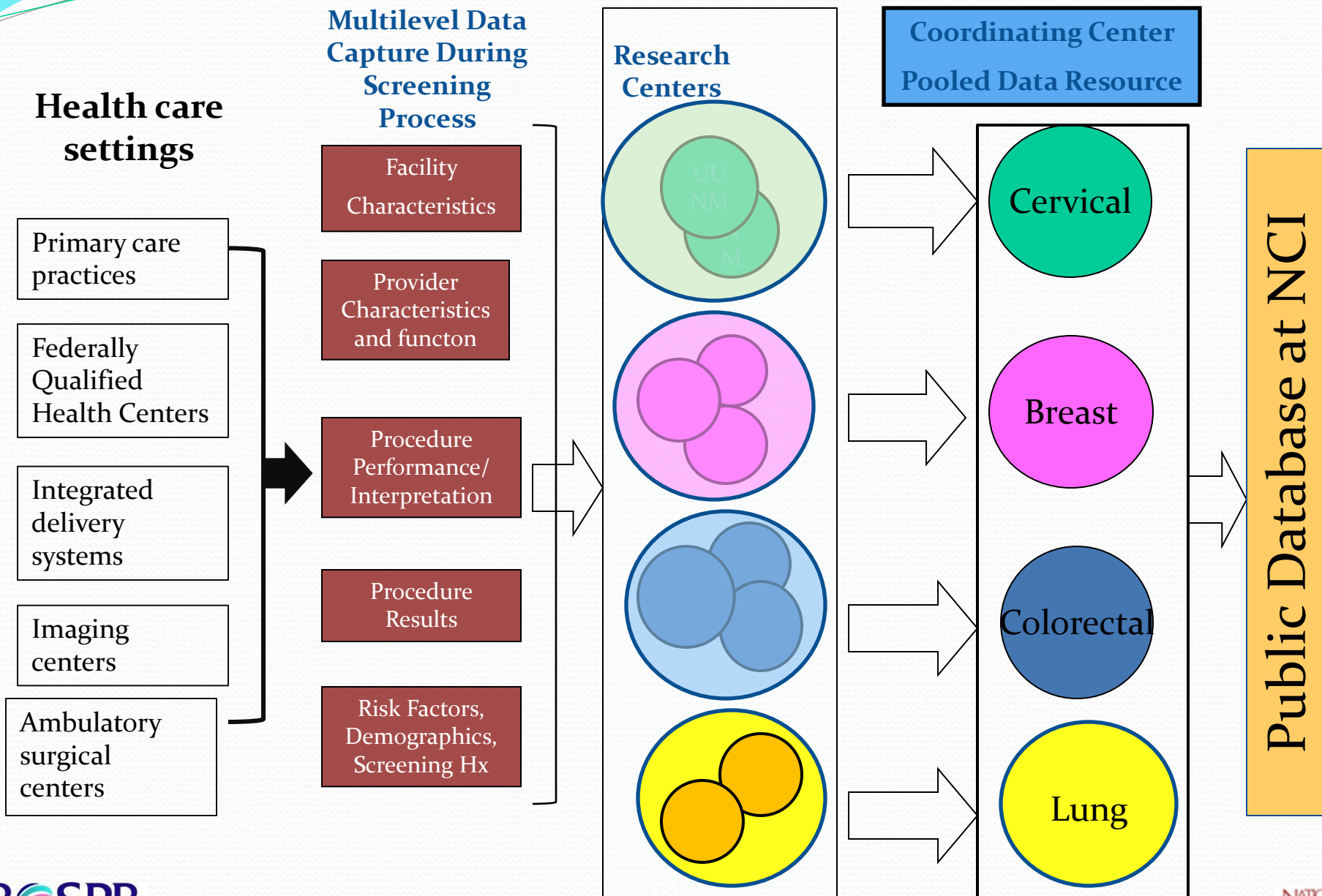
Table of RUCA_calc by PRC within organ group										
Washington University Rural Urban Commute Area indicator (version 2.0)	PRC within organ group									Total
	Breast			Colorectal			Cervical			
	Dart/B&W	UPenn	UVT	GHRC	Kaiser	UTSW	GHRC	Kaiser	UTSW	
RUCA database does not list ZIP	89	164	1879	4893	1827	11	4101	2271	39	.
PPT without ZIP	296	1036	793	285	28710	8	346	37946	30	.
1: Metropolitan	103407 83.8	134064 99.7	29927 26.9	219773 96.5	2899357 99.0	66823 100.0	314266 96.5	3800674 99.2	179465 100.0	7747756
2: Micropolitan	13247 10.7	317 0.2	22493 20.2	6007 2.6	14372 0.5	12 0.0	8508 2.6	16445 0.4	37 0.0	81438
3: Rural	6787 5.5	103 0.1	58740 52.8	1900 0.8	14642 0.5	5 0.0	2897 0.9	16058 0.4	12 0.0	101144
Total	123441	134484	111160	227680	2928371	66840	325671	3833177	179514	7930338

Insurance Coverage & PROSPR Centers

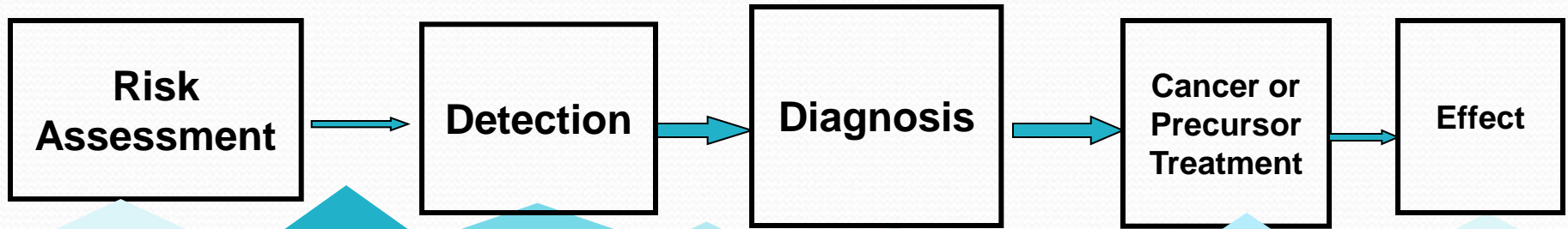
Table of Insurance by PRC within organ group											
Insurance specification (first non-missing)	PRC within organ group										
	Breast			Cervical				Colorectal			Total
	Dart/BW	UPenn	UVt	GHC	Kaiser	UNM	UTSW	GHC	Kaiser	UTSW	
Missing/Unknown	4232	2565	113832	0	4315	343109	1830	0	2020	6	.

1: Medicaid	5735 5%	16944 13%	0	8391 3%	115329 3%	0	39636 22%	445 0%	28847 1%	5914 9%	221241
2: Medicare	20084 17%	22625 17%	0	44054 13%	561761 15%	0	4217 2%	72019 31%	930816 31%	5129 8%	1660705
3: Commercial	82158 69%	92456 69%	0	270873 82%	3191989 82%	0	8596 5%	156077 67%	1997225 68%	3760 6%	5803134
4: Other	3629 3%	507 0%	0	6800 2%	0 0%	0	41503 23%	4317 2%	0 0%	1239 2%	57995
5: Uninsured/ medical assist	7988 7%	587 0%	0	0 0%	0 0%	0	83801 47%	0 0%	0 0%	50811 76%	143187
Total	119594	133119	0	330118	3869079	0	177753	232858	2956888	66853	7886262

PROSPR II: Data Infrastructure



We know more about parts of the process



Characterize populations at low risk for CRC

Personalize with BCI

Communication strategy

Primary Care Integrated Risk assess tool

CE DBT vs Digital

Current practice of self-sampling

Molec Char of FIT-missed C-oscopy Qual

Molecular & Morph DCIS

Breast Density, collagen reorg & survival

Ben & Harms of personalized DCIS Personalized risk & next steps for adenoma

CE of current practice

Long-term CE of risk stratified screen

Failure analysis

2 CER of FIT v C-oscopy

Organization & clinic-level factors

Breast	X	X	X		X		X	X
Cervical	O	O	X					X
CRC	X	O	X				X	X

Zapka et al 2003

Population diversity differs across centers

	Breast			Cervical				Colorectal		
	Site A	Site B	Site C	Site D	Site E	Site F	Site G	Site D	Site E	Site G
	%	%	%	%	%	%	%	%	%	%
White	79	53	95	74	45	59	10	80	55	18
Black	8	36	0	5	9	2	25	4	9	37
Hispanic	9	2	2	6	29	34	61	4	22	39
Asian/PI	4	4	1	11	15	1	3	8	13	6
Am.Ind./AK Native /Other	0	5	2	5	1	4	0	3	1	0