Changing Breast Cancer Outcomes

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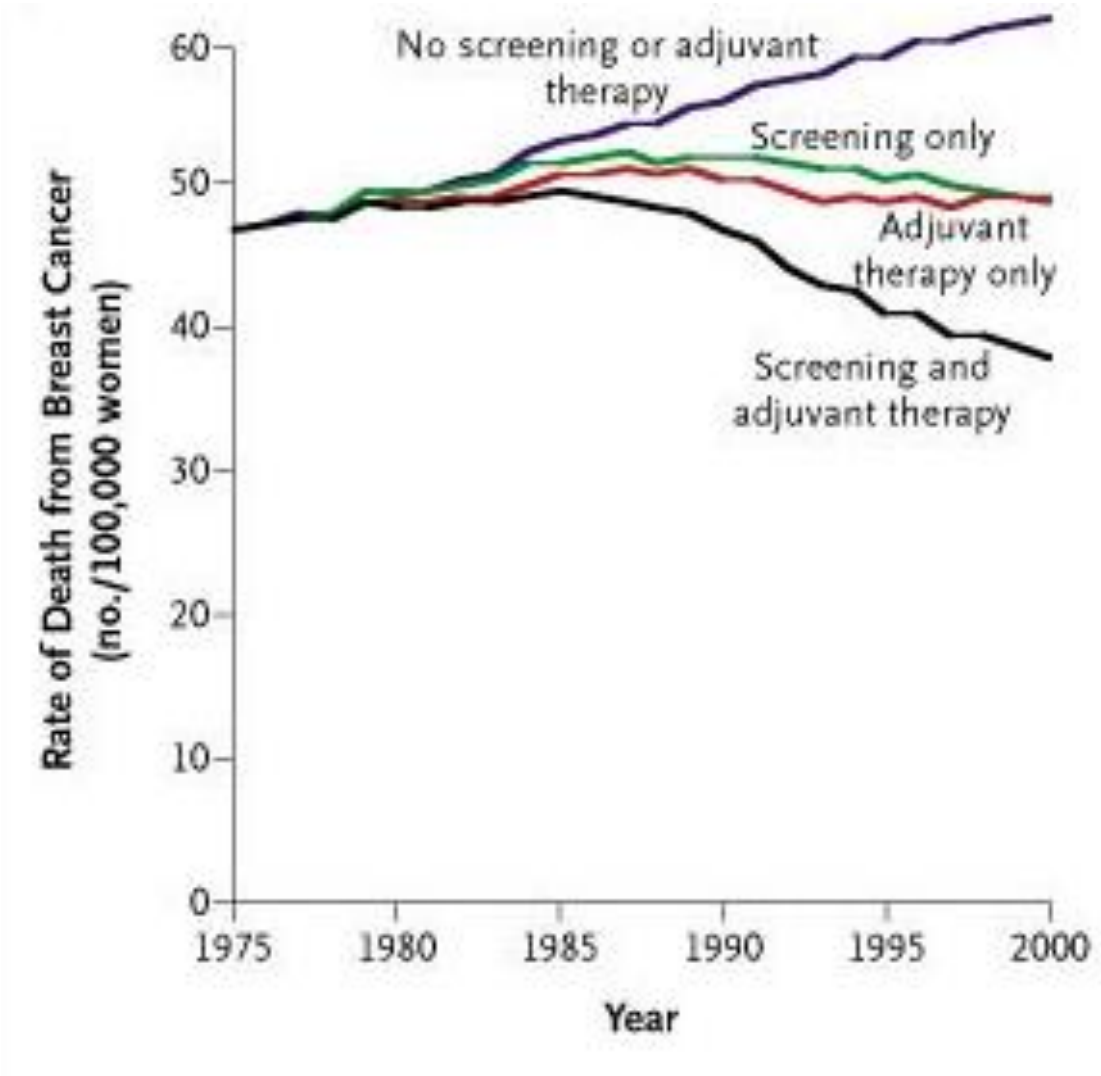
University of Minnesota
Comprehensive Cancer Center designated by the National Cancer Institute

Better Outcomes Due To More Screening and More Medical Therapy



Berry, et al. N Engl J Med 353:1784 2005

Goals For Medical Adjuvant Therapy

- Identify patients with highest likelihood of dissemination of micrometastatic disease to distant organs
- Exploit known targets in breast cancer
  - Estrogen receptor-α – “hormone” therapy
  - DNA synthesis - chemotherapy
  - HER2 oncogene – trastuzumab
- Identify individual risk for each patient to provide appropriate therapy
  - De-escalate therapy for low risk patients
  - Precision therapy for high risk patients

Oncotype DX 21 Gene Recurrence Score (RS) Assay

16 Cancer and 5 Reference Genes From 3 Studies

PROLIFERATION
Ki-67
STK15
Survivin
Cyclin B1
MYBL2

ESTROGEN
ER
PR
Bcl2
SCUBE2

GSTM1

BAG1

INVASION
Stromolysin 3
Cathepsin L2

CD68

HER2
GRB7
HER2

REFERENCE
Beta-actin
GAPDH
RPLPO
GUS
TFRC

RS = + 0.47 x HER2 Group Score
- 0.34 x ER Group Score
+ 1.04 x Proliferation Group Score
+ 0.10 x Invasion Group Score
+ 0.05 x CD68
- 0.08 x GSTM1
- 0.07 x BAG1

Category	RS (0 – 100)
Low risk	RS < 18
Int risk	RS ≥ 18 and < 31
High risk	RS ≥ 31

Paik, et al. N Engl J Med 351:2817 2004

TAILORx Methods: Treatment Assignment & Randomization

Accrued between April 2006 – October 2010

Preregister - Oncotype DX RS (N=11,232)

↓

Register (N=10,273)

ARM A: Low RS 0-10
(N=1629 evaluable)
ASSIGN
Endocrine Therapy (ET)

Mid-Range RS 11-25
(N=6711 evaluable)
RANDOMIZE
Stratification Factors: Menopausal Status, Planned Chemotherapy, Planned Radiation, and RS 11-15, 16-20, 21-25

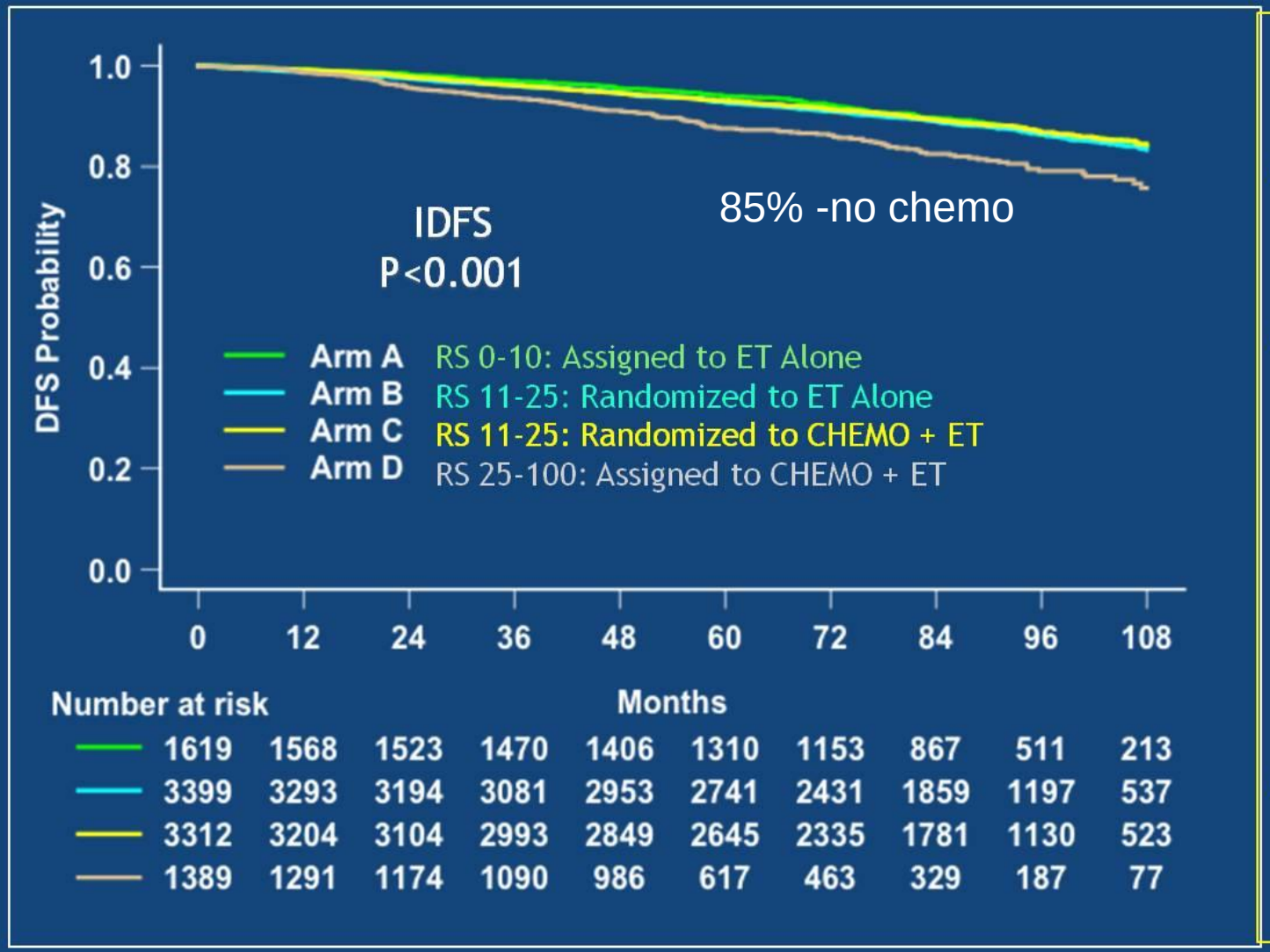
ARM D: High RS 26-100
(N=1389 evaluable)
ASSIGN
ET + Chemo

ARM B: Experimental Arm
(N=3399)
ET Alone

ARM C: Standard Arm
(N=3312)
ET + Chemo

Sparano, et al. N Engl J Med 2018 PMID: 29860917

TAILORx Results - ITT Population: All Arms (A,B,C & D)



9-Year Event Rates

- **RS 0-10 (Arm A)**
  - 3% distant recurrence with ET alone
- **RS 11-25 (Arms B & C)**
  - 5% distant recurrence rate overall
  - ≤ 1% difference for all endpoints
    - IDFS (83.3 vs. 84.3%)
    - DRFI (94.5 vs. 95.0%)
    - RFI (92.2 vs. 92.9%)
    - OS (93.9 vs. 93.8%)
- **RS 26-100 (Arm D)**
  - 13% distant recurrence despite chemo + ET

Sparano, et al. N Engl J Med 2018 PMID: 29860917

CALGB INTERSPORE ACRIN NCICB

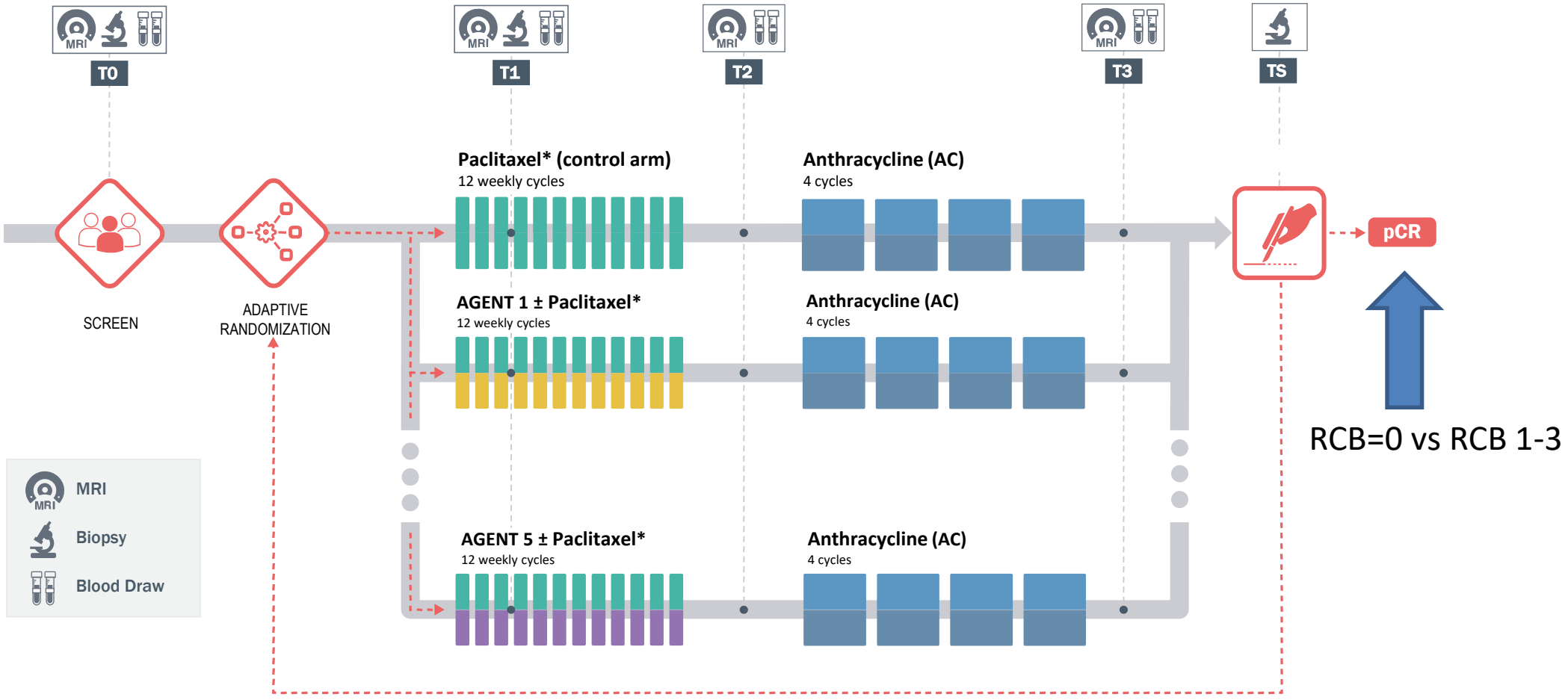
CALGB 150012/150007 and ACRIN 6657

Investigation of
Serial studies to
Predict
Your
Therapeutic
Response with
Imaging and Molecular
Ana-
Lysis

I SPY WITH MY LITTLE EYE ...
A BIO-MARKER BEGINING WITH X...

P.I. – Laura Esserman, M.D. UCSF

I-SPY 2 TRIAL Study Design



HR+/HER2- patients with low-risk 70- gene (MammaPrint) Scores are not enrolled in I-SPY2
Agilent 44K IDE

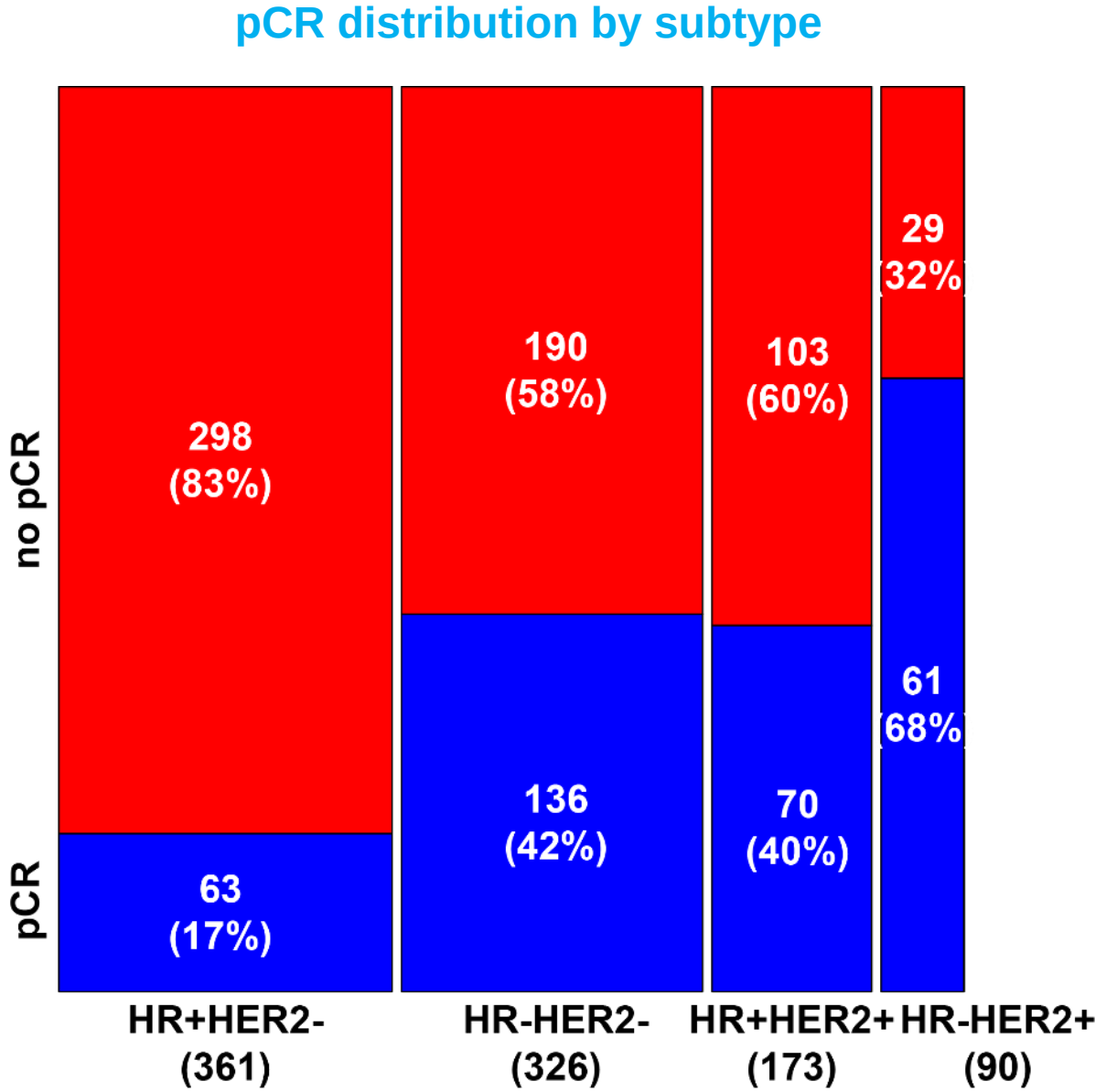
EFS Dataset

Updated I-SPY 2 EFS/DRFS data

- 950 patients
- 3.8 years median follow-up

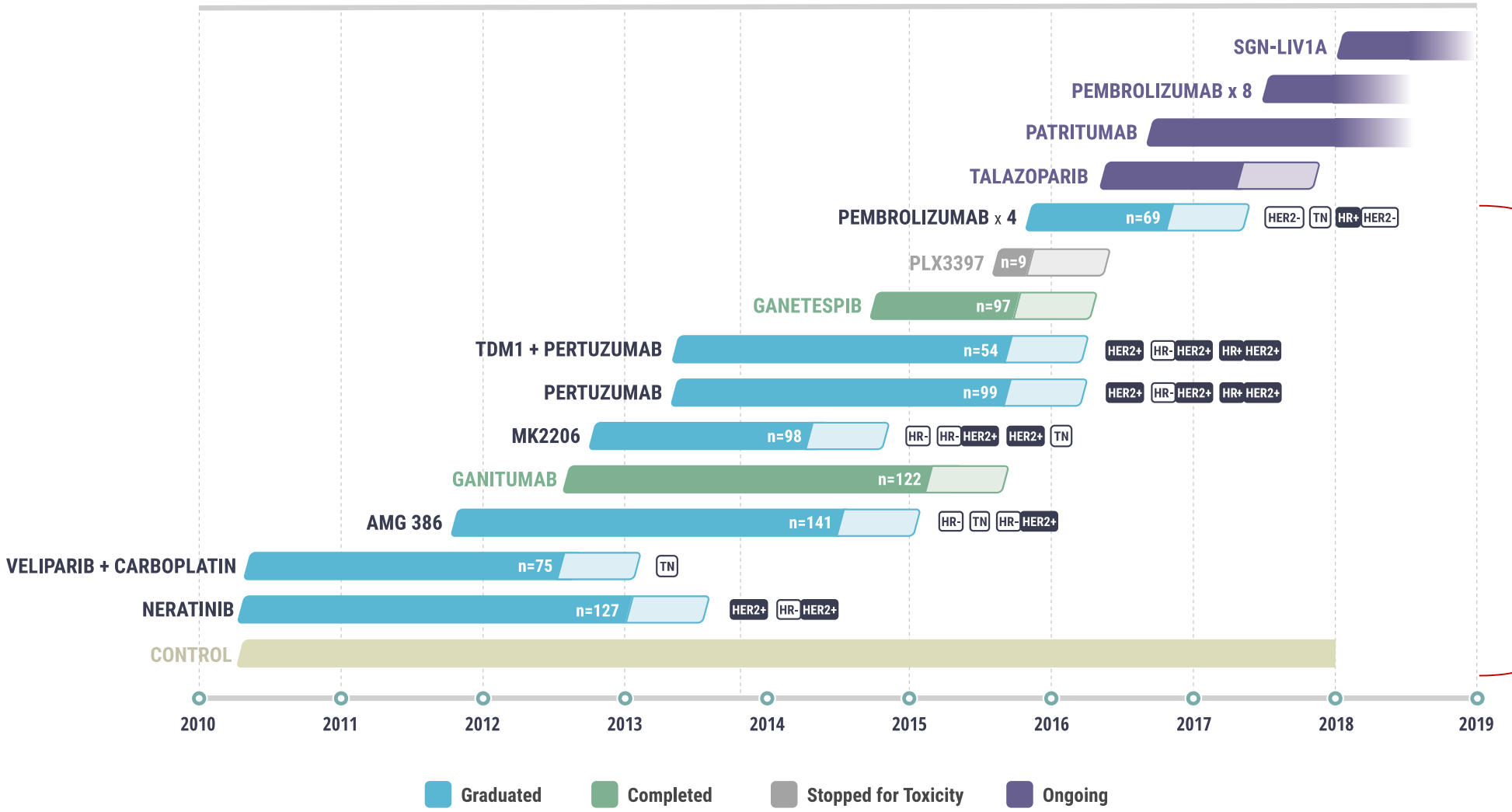
pCR rates differ by subtype

- HR+ rates have lowest pCR



Yee, SABCS 2017

Agent Timeline

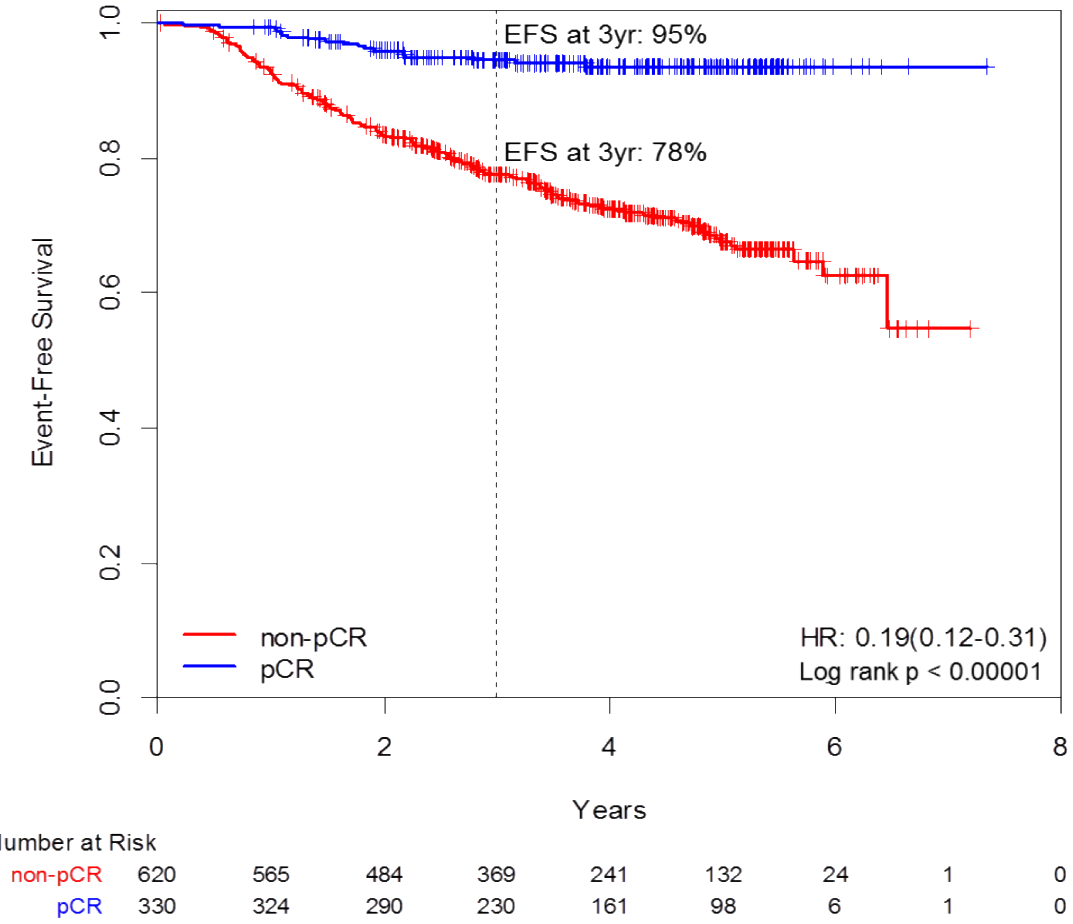


11 Agent Combinations Included in this analysis, including control

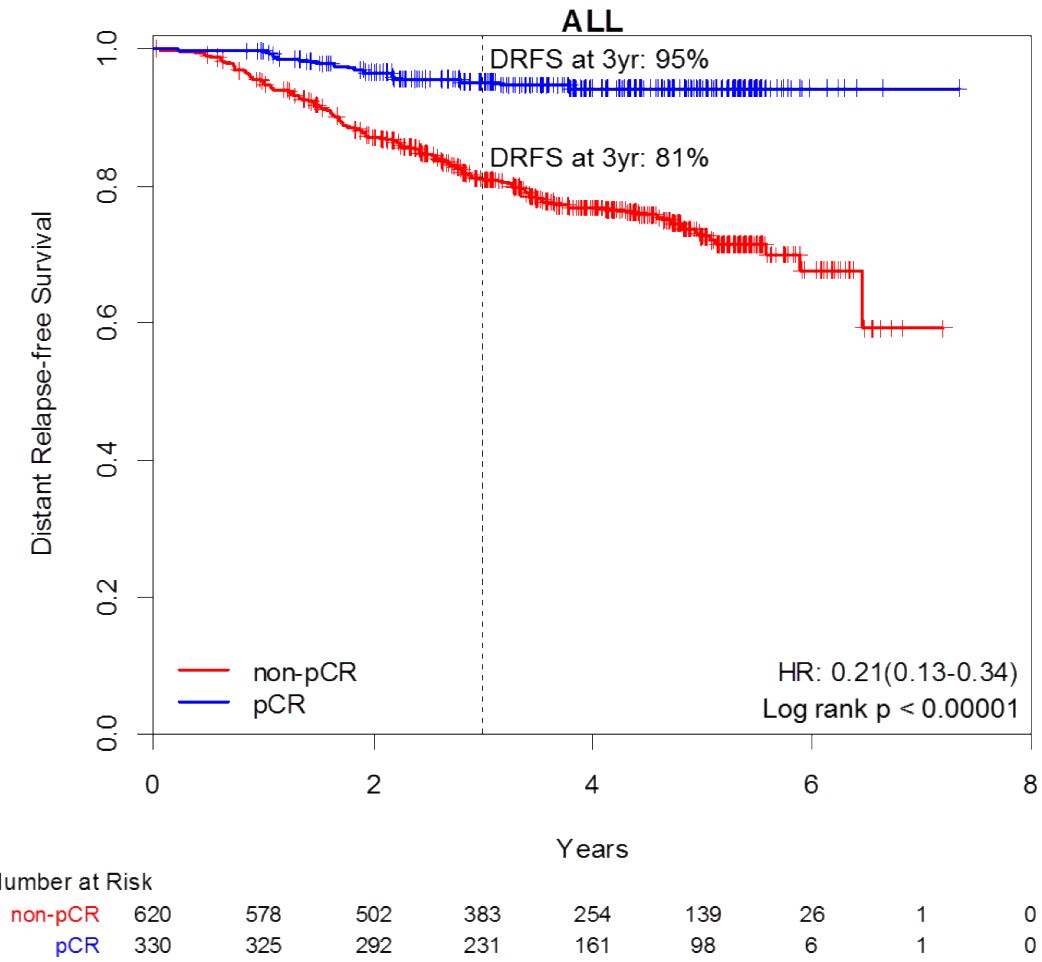
Yee, et al. submitted

pCR is a highly significant predictor of EFS and DRFS

EFS



DRFS

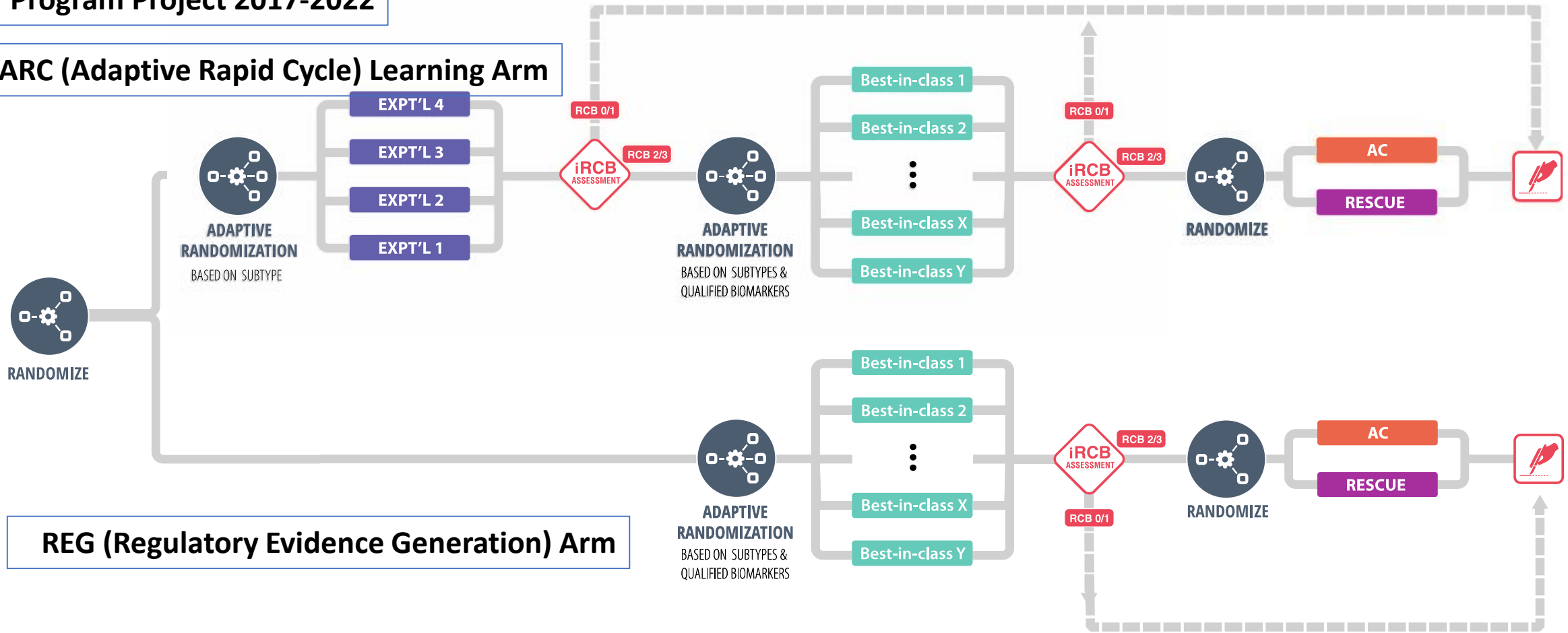


Yee, et al. submitted

I-SPY 2+ Draft Design: Maximizing the chance of achieving pCR

Program Project 2017-2022

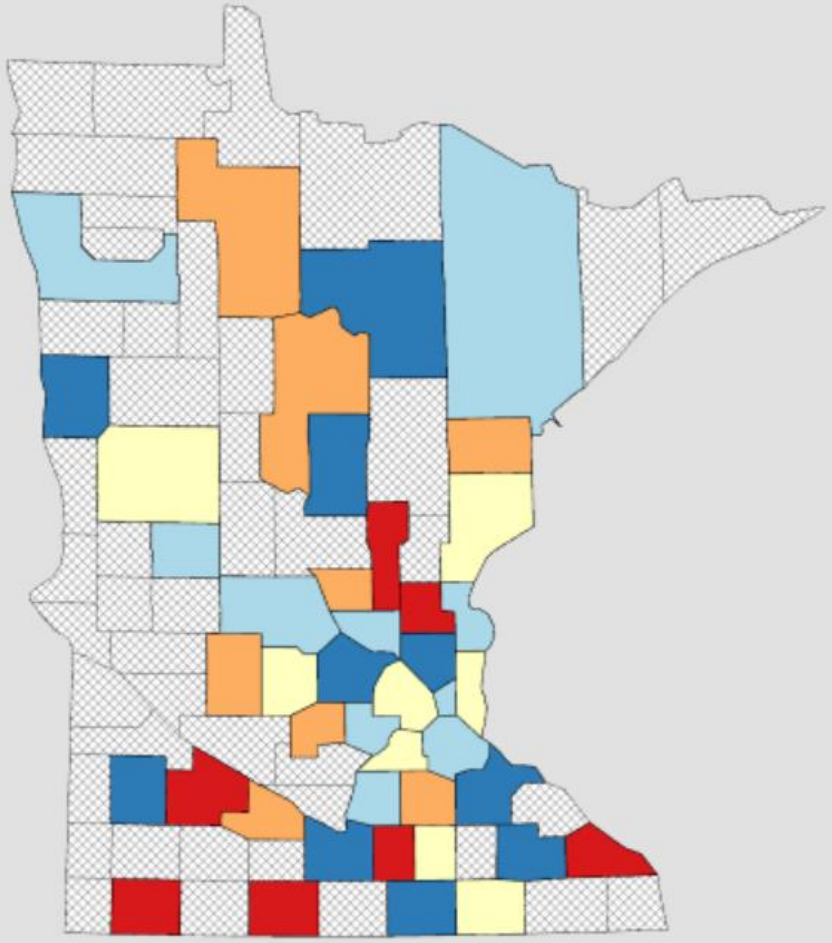
ARC (Adaptive Rapid Cycle) Learning Arm



REG (Regulatory Evidence Generation) Arm

Block A | Block B | Block C

Death Rates for Minnesota by County
Breast, 2012 - 2016
All Races (includes Hispanic), Female, All Ages



Age-Adjusted
Annual Death Rate
(Deaths per 100,000)

Quantile Interval

- 14.2 to 17.1
- > 17.1 to 18.4
- > 18.4 to 20.0
- > 20.0 to 23.8
- > 23.8 to 28.7
- Suppressed *

United States
Rate (95% C.I.)
20.6 (20.5 - 20.7)

Minnesota
Rate (95% C.I.)
18.2 (17.5 - 18.8)

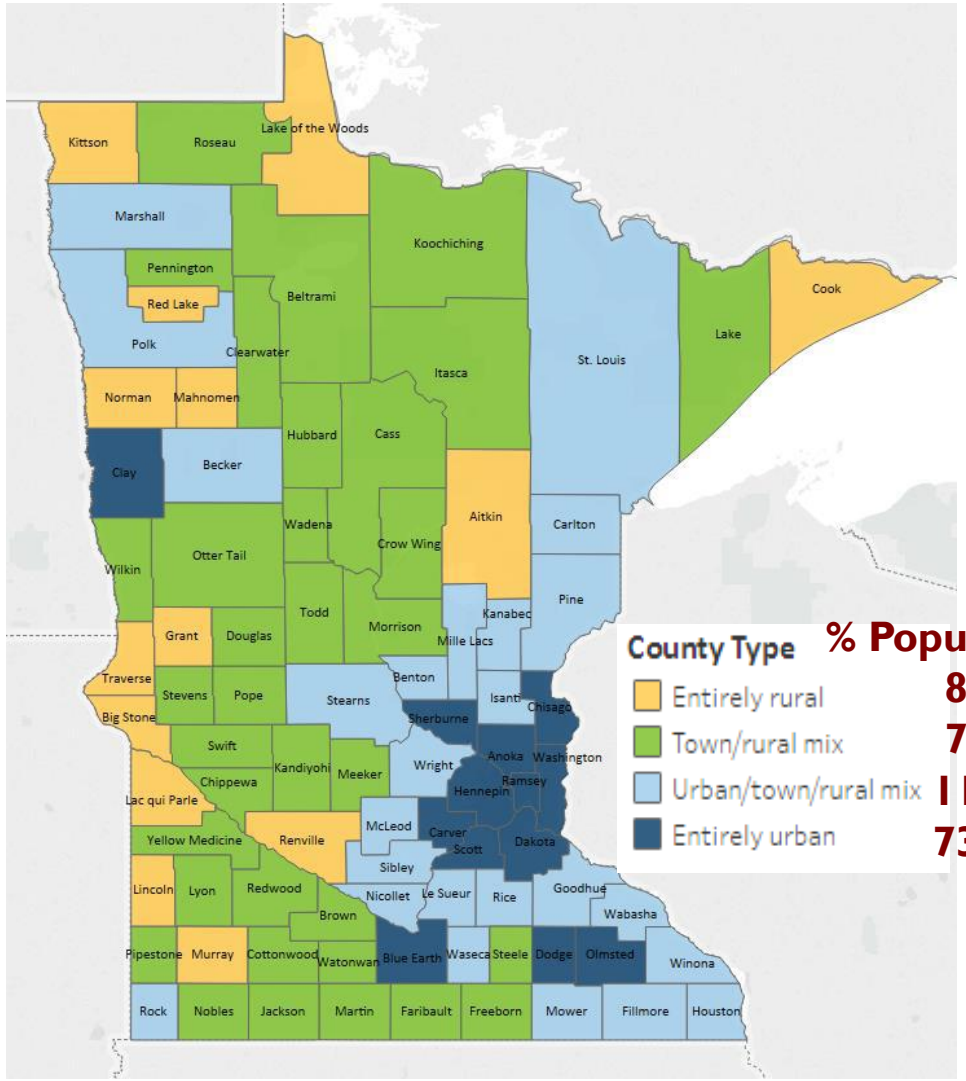
Healthy People 2020
Goal C-3
20.7

https://statecancerprofiles.cancer.gov/map/map.withimage.php?27&county&001&055&00&2&02&0&1&5&0#results

Potential Cancer Disparities In Minnesota

Special Populations

- Largest urban population of Hmong in the world (~90,000) is in the Twin Cities
- Largest Somali-American population in the country (~40,000)
- 11 Federally recognized American Indian tribes (~68,000)
- 26% rural – rural/mix



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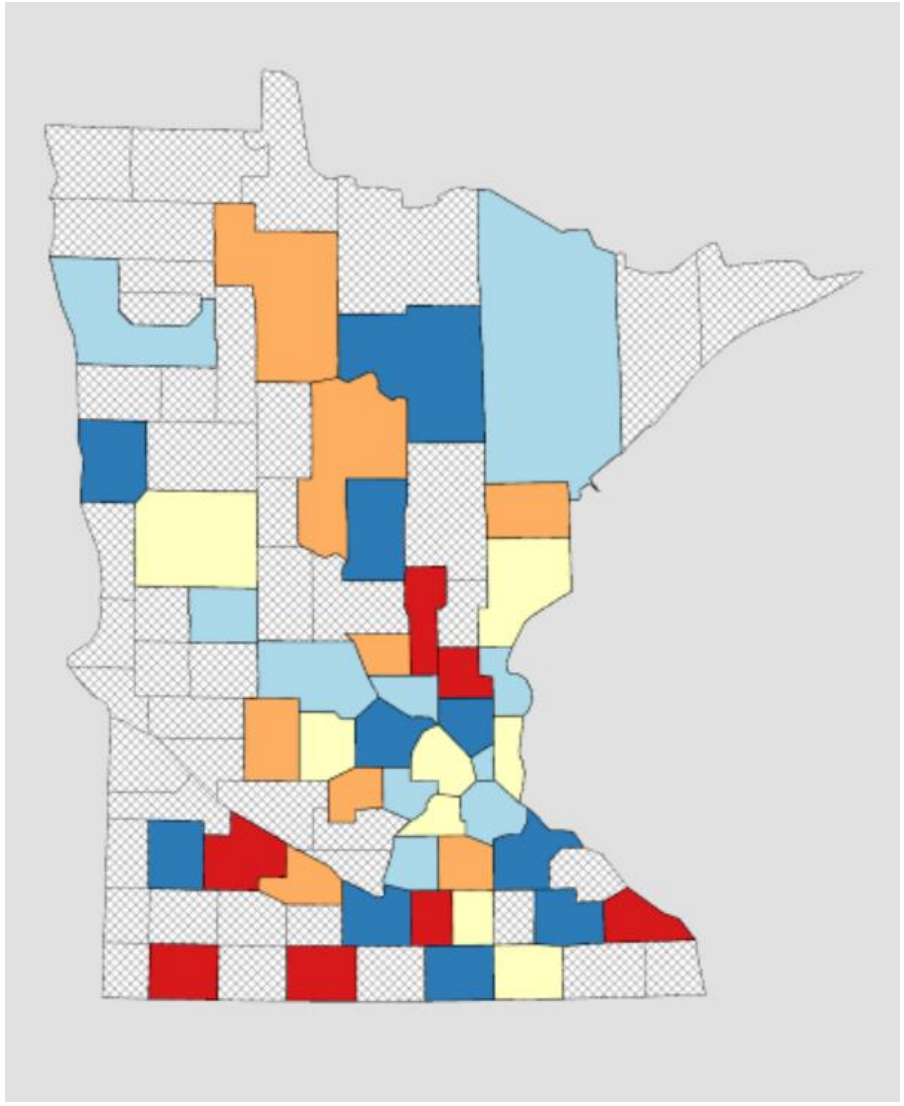
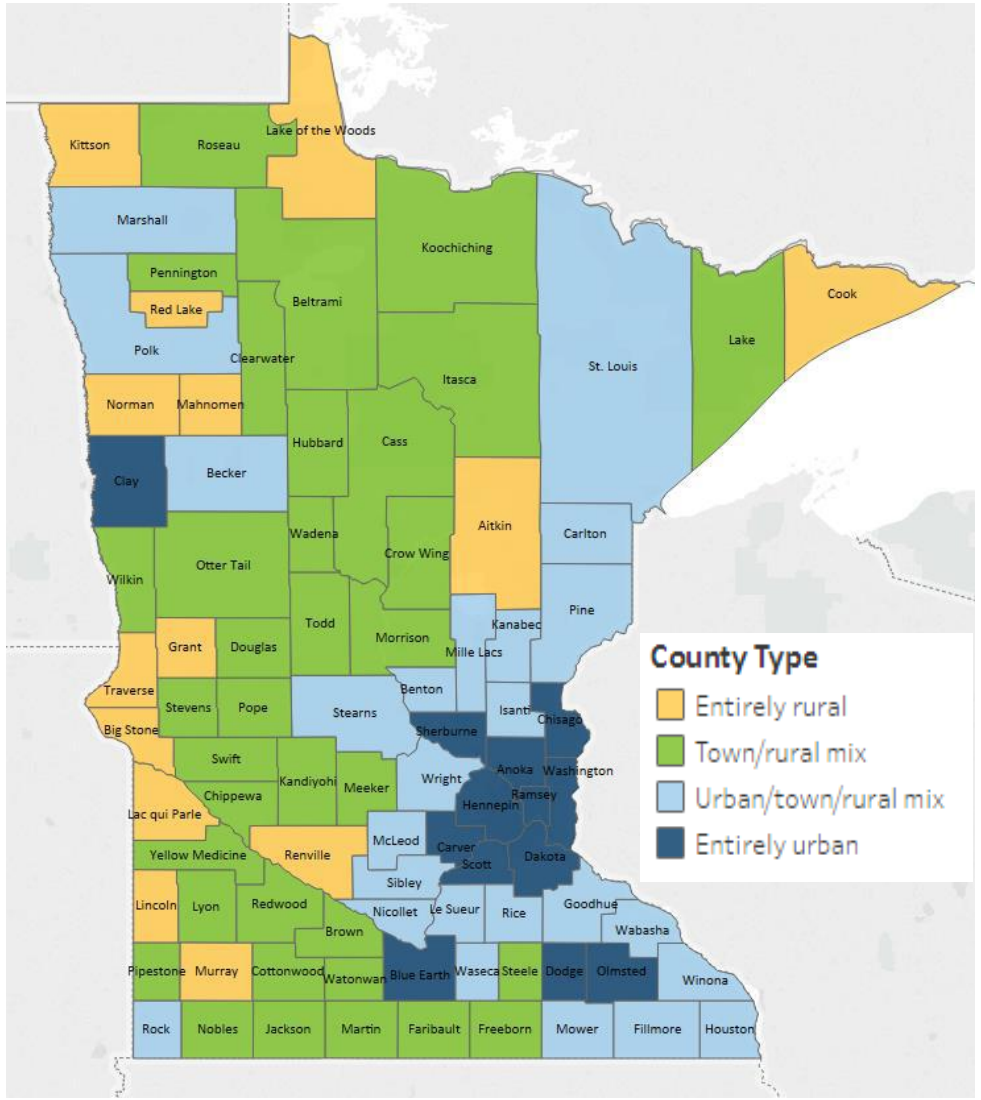
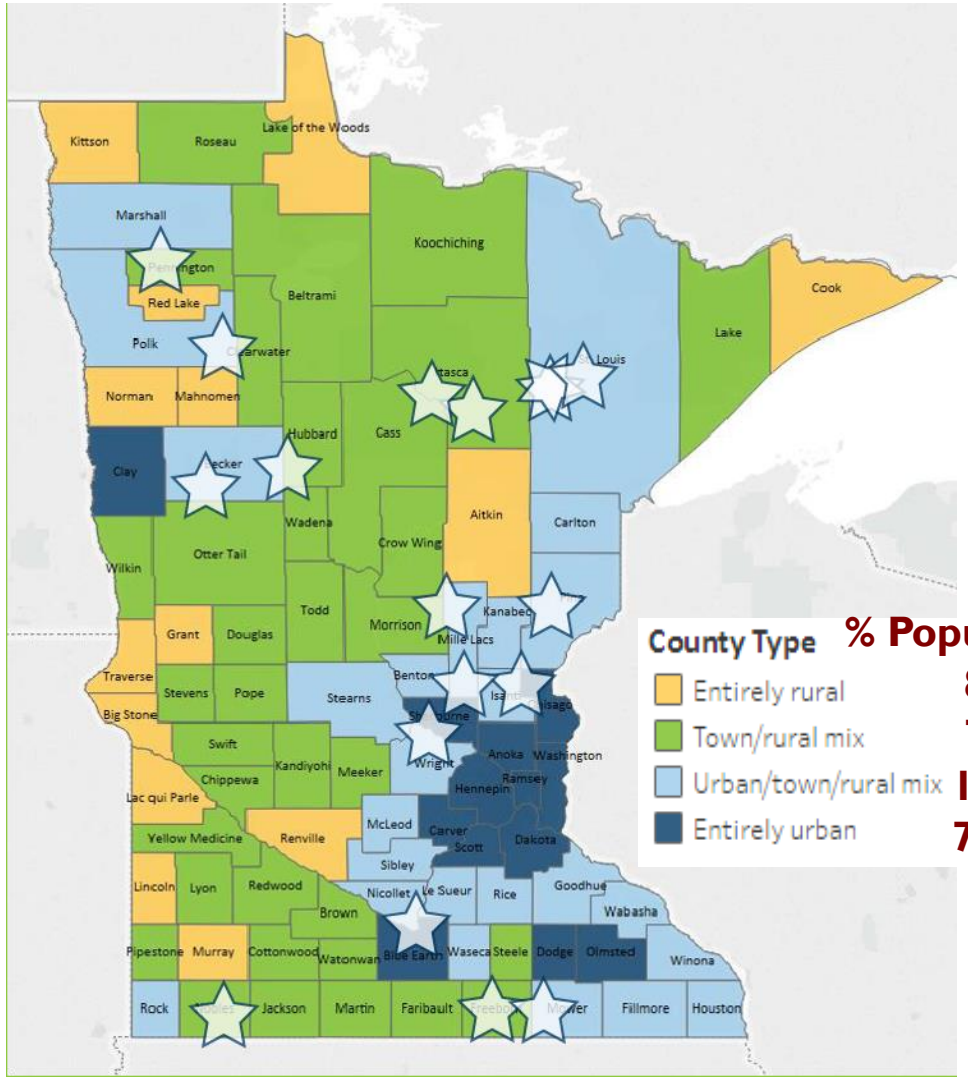




Minnesota Cancer Clinical Trials Network

- Supported through MNDrive - $4M year
- Engaged
  - Mayo Clinic Cancer Center
  - Metro MN NCORP
  - Sanford Health NCORP
  - Essentia Health CCRP
  - Mille Lacs Band Ojibwe
  - Hormel Institute
  - Fairview Health Services
- Enrolled 317 patients to date
  - 12% rural
  - 43% town/rural
  - 45% urban/town/rural



What's Next For Breast Cancer?

- Better individualized markers of:
  - Risk to aid mammographic screening
    - WISDOM trial
  - Predictive factors to select "right sized" treatment
- New and novel drugs
- Innovation in clinical trial design
- Inclusion of "ignored" populations