A Novel Data Linkage to Examine the Long Term Adverse Consequences of Cancer Treatment: The SWOG-Medicare Database

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Outline

- **Introduction** to outcomes research in SWOG
- **Motivation** for linking SWOG database to Medicare claims
- **Description** of SWOG-Medicare linkage
- **Examples** of studies conducted using the linkage
- **Future Plans**

The SWOG Cancer Research Network

- SWOG is a national clinical trials consortium sponsored by NCI
- Member of the NCI's National Clinical Trials Network (NCTN) and its Community Oncology Research Program (NCORP)
- About SWOG:
  - Originated in 1956
  - One of the 4 NCI-sponsored adult cancer network groups
  - 12,000 investigators
  - 1,000 hospitals, clinics, and cancer centers worldwide
  - Members in 47 states and 6 countries
  - >250,000 patient records

Outcomes Research in SWOG

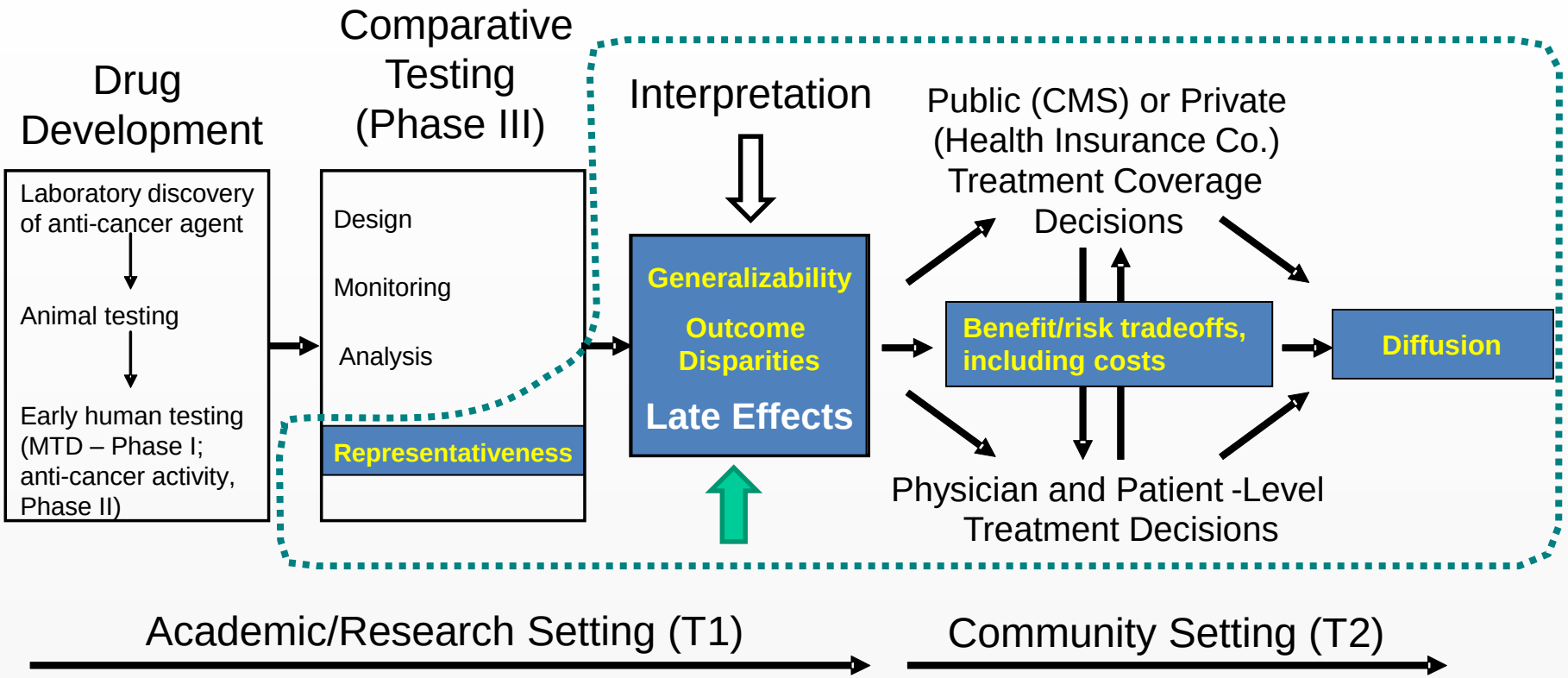
- Outcomes and cancer disparities research conducted under:
  - Cancer Care Deliver Research committee (Co-Chairs: Dawn Hershman, Scott Ramsey)
  - Hope Foundation Translational Medicine Grant (Unger)

Meta-Data or “Big Data” Strategies

Using data from a national clinical trials database, in combination with…

- Registry (SEER)
- Life-table
- Census
- Publication or citation data
- Medicare claims

Conceptual Model: Study to Diffusion of New Cancer Therapy



Clinical Trial Data for Outcomes Research: Advantages

- Prospective data collection
- Collection of clinical prognostic factors
- Detailed, protocol specified treatment information
- Acute toxicity and severity
- Recurrence/progression
- Implicit access to care to alleviate confounding when examining cancer disparities

Clinical Trial Data for Outcomes Research: Disadvantages

- Limited utilization data (beyond protocol specified therapy)
- No cost data
- No adverse events after treatment stops
- Limited long-term follow-up

Prospective Late Effects Studies

- Re-consent patients in FU to new study
- S9342: Examined patient cardiac function at 5-8 years after registration to a prior large, adjuvant breast cancer trial (S8897)*
- 954 potentially eligible patients (alive in FU)
- N=156 were registered and evaluable

…Enrollment rate = 16%

**** Ganz et al., JCO, 2008***

SWOG-Medicare Linkage

Program objectives

- To link the SWOG clinical trial records to Medicare claims to leverage the advantages of both databases
- To conduct late effects, treatment utilization, and cost studies in timely fashion at low cost

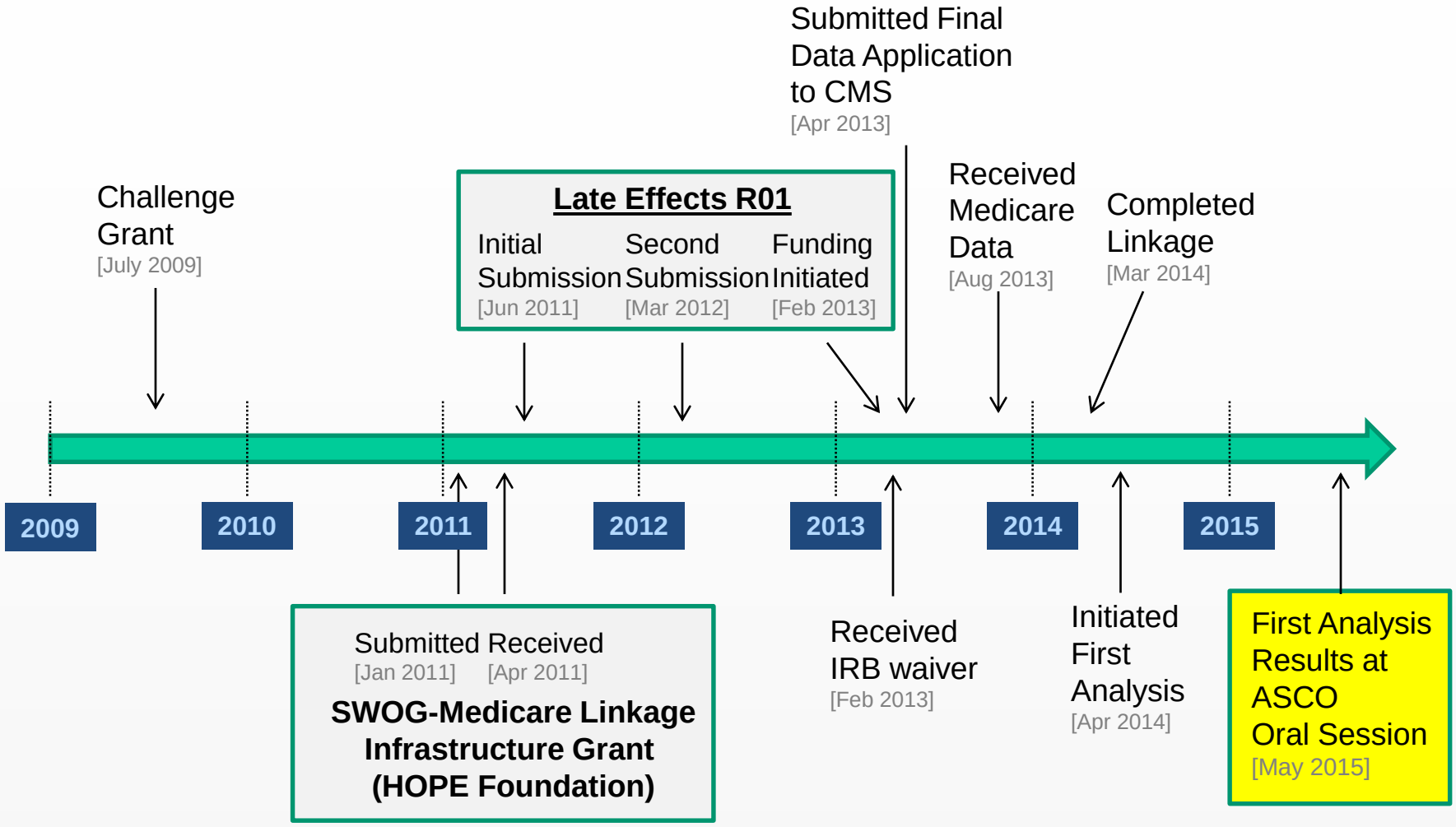
The Linked SWOG-Medicare Database

- Clinical trials capture demographics; tumor and clinical prognostic factors; treatment and dose; short term toxicities; and recurrence and survival
- Medicare claims data (based on ICD-9, HCPCS, and CPT codes) provides long-term follow-up with underlying illnesses, comorbid conditions, new diagnoses; treatment utilization data; and cost data
- Advantage of random assignment for treatment comparisons from a specific study; limits confounding

Linkage Statistics

- Submitted 115,623 records for linkage for 14-year period 1999-2012
- Records submitted for patients of all ages
  - Allows patients to “age into” the Medicare cohort
- Linkage rate among all SWOG patients with required identifiers: **71%**
  - Compare to **16%** from prior prospective late effects study (S9342)

Project Timeline



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EXAMPLE: Late Effects of ADT in S9346

JAMA Oncology, 2016

Research

Original Investigation

Adverse Health Events Following Intermittent and Continuous Androgen Deprivation in Patients With Metastatic Prostate Cancer

Dawn L. Hershman, MD, MS; Joseph M. Unger, PhD; Jason D. Wright, MD; Scott Ramsey, MD, PhD; Cathee Till, MS; Catherine M. Tangen, PhD; William E. Barlow, PhD; Charles Blanke, MD; Ian M Thompson, MD; Maha Hussain, MD

IMPORTANCE Although intermittent androgen-deprivation therapy (ADT) has not been associated with better overall survival in prostate cancer (PC), it has the potential for lower adverse effects. To our knowledge, the incidence of long-term adverse health events has not been reported.

OBJECTIVE To examine long-term late events in elderly patients randomized to intermittent or continuous ADT to determine whether late cardiovascular and endocrine events would be

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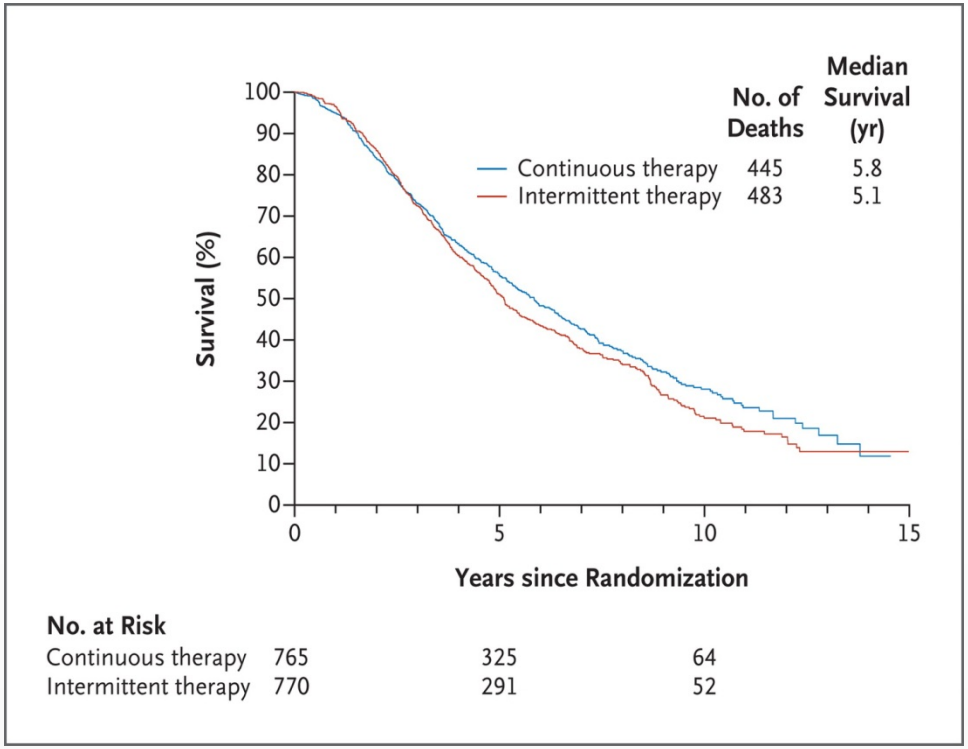
Supplemental content at jamaoncology.com

Original Study Objectives*

- To assess whether intermittent ADT was non-inferior to continuous ADT with respect to overall survival
- To assess whether quality of life was different at 3 months after randomization

S9346 Results*



HR [IAD/CAD] = 1.10 (95% CI: 0.99-1.23)

- Overall survival results “statistically inconclusive”
- Suggest that “IAD may compromise survival”
- IAD associated with better quality of life at 3 months but not thereafter
  - Erectile dysfunction (p<.001)
  - Mental health (p=.003)

**** Hussain et al., NEJM, 2013***

Late Effects for S9346

- Objective: To examine late effects by treatment for patients randomized to IAD vs. CAD on S9346 using the linked SWOG-Medicare database
- Hypothesis: Late cardiovascular and endocrine effects would be **lower** in patients on **intermittent ADT***

*** Calais da Silva FE et al., Eur Urol, 2009; Calais da Silva FE et al., Eur Urol, 2014**

Results

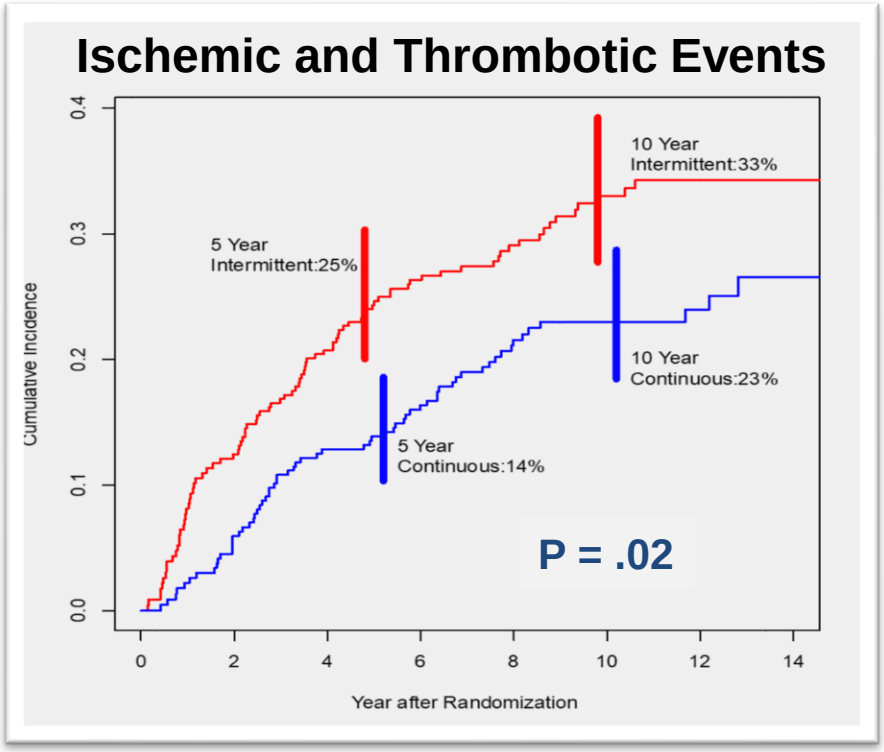
- N=1134 U.S. based patients eligible and randomized
- N=636 (56% of total) evaluable for late effects through the Medicare claims linkage
  - Had ≥1 year continuous Medicare coverage and no HMO
- No evidence that survival patterns by arm differed between those with and without Medicare claims (interaction p = .79)
- No imbalances by arm for important demographic or clinical factors

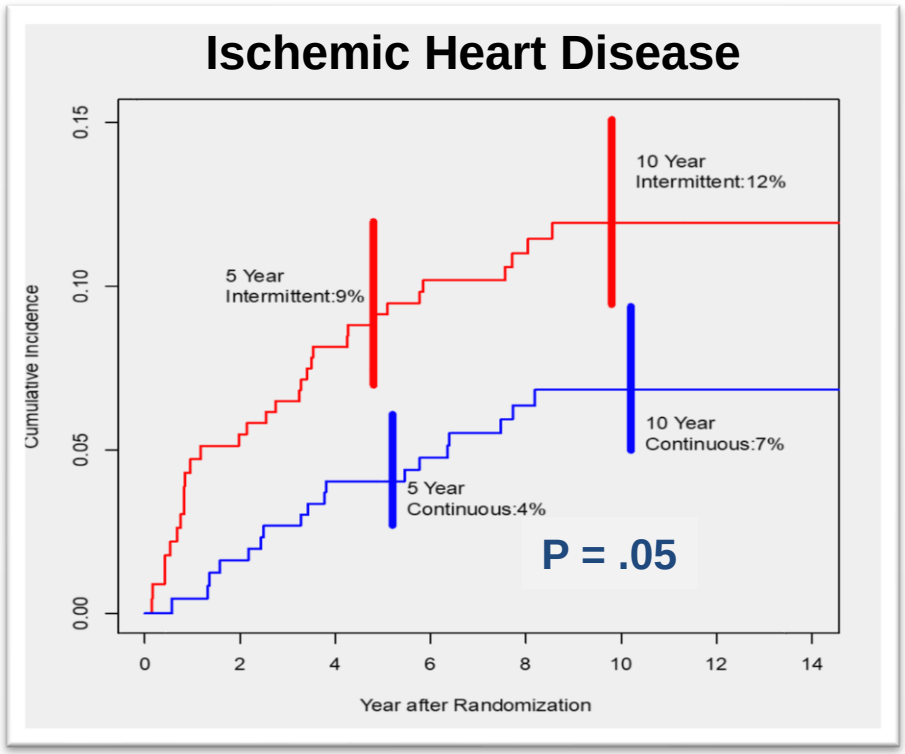
Multivariable Regression Results

	Hazard Ratio	P-Value
Ischemic/Thrombotic	**0.69**	**.02**
Acute MI	0.80	.42
Ischemic Heart Disease	**0.55**	**.05**
Thrombosis	0.79	.28
Endocrine	1.06	.67
Diabetes	1.08	.69
Hypercholesterolemia	1.00	1.00
Obesity	1.49	.20
Osteoporosis	1.18	.35
Fracture	1.17	.43
All Bone	1.16	.32
Sexual Dysfunction	1.29	.46
Dementia	1.97	.07
Depression	0.92	.69

1 = CAD, 0 = IAD

Cumulative Incidence





- Intermittent - Continuous

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Conclusions

- Contrary to the hypothesis, our findings suggested that patients on the CAD arm do not, on average, have a worse late effects profile
- In some instances IAD may even be worse

SWOG-Medicare Linkage: Publications

- "Adverse Health Events Following Intermittent and Continuous Androgen Deprivation in Patients With Metastatic Prostate Cancer" – Hershman et al., ***JAMA Oncol***, 2016
- "Long-term Consequences of Finasteride vs Placebo in the Prostate Cancer Prevention Trial" – Unger et al., ***JNCI***, 2016
- "Comorbidities and Risk of Chemotherapy-Induced Peripheral Neuropathy Among Participants 65 Years or Older in Southwest Oncology Group Clinical Trials" – Hershman et al., ***JCO***, 2016
- "History of Diabetes and Survival Outcome Among Participants 65 or Older in SWOG Clinical Trials" – Hershman et al., ***JCO CCI***, 2017
- "Using Medicare Claims to Examine Long-term Prostate Cancer Risk of Finasteride in the Prostate Cancer Prevention Trial" – Unger et al., ***JNCI***, 2018
- "Osteoporosis in colorectal cancer survivors: analysis of the linkage between SWOG trial enrollees and Medicare claims" – Barzi et al., ***Arch Osteoporos***, 2019
- "Association of Cardiovascular Risk Factors With Cardiac Events and Survival Outcomes Among Patients With Breast Cancer Enrolled in SWOG Clinical Trials" – Hershman et al., ***JCO***, 2018
- "Healthcare utilization and cost of care in elderly breast cancer patients enrolled in SWOG clinical trials" – Hershman et al., ***Breast Cancer Res Treat***, 2020
- "Long-term Complications of Prostate Cancer Treatment" – Unger et al., 2020, submitted

Common Limitations

- Risk of misclassification
  - Potential that not all patients had the assigned complication
- Medicare claims lack data on severity
  - Some of these complications were likely mild and not life-threatening
- All the patients are enrolled in trials, therefore the generalizability of the results may be somewhat limited
- Inferences limited to older patients since *Medicare* claims

Conclusions

- Cancer clinical trials involve following a large number of patients for many years
- Costs of conducting such studies are very high
- Medicare claims data can be used to augment detection of long term outcomes and late effects at much reduced cost

Future Plans

- Receiving new Medicare claims data through 2018 early next year
- Potential to link all payer claims databases to enrich linkage to younger patients

Acknowledgements

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- The HOPE Foundation: Obtaining Medicare Claims Data for Use in SWOG Comparative Effectiveness Studies, 2011-2013 [Hershman, Unger (Co-PI)]
- NIH (1R01CA166084-01A1): Using SWOG-Medicare Database To Evaluate Long-Term Toxicities Of Cancer Survivors, 2013-2017 [Hershman; Unger (Co-I)]
- NIH (2 U01 CA182883-06A1): PCPT and SELECT Cohorts: Core Infrastructure Support for Cancer Research, 2019-2024 [Tangen]