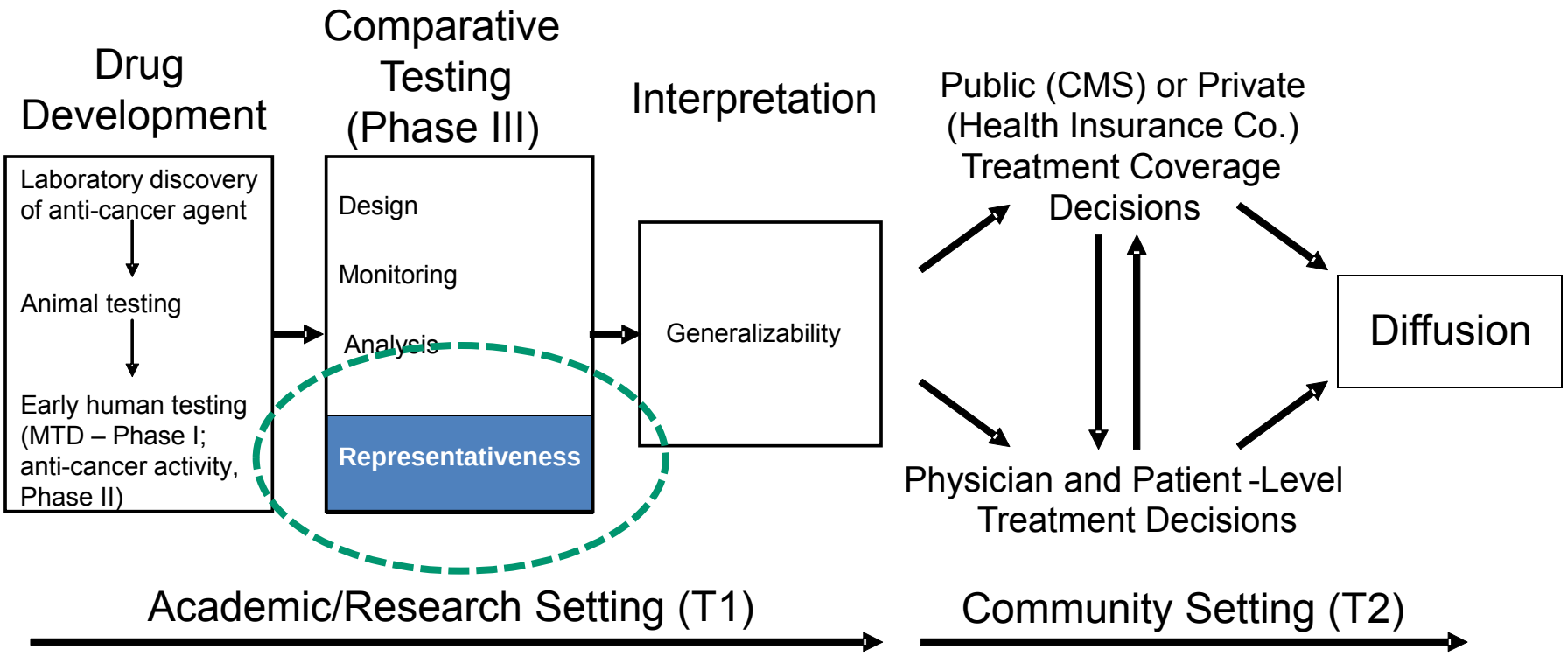
Models to Identify and Support Clinical Trial Participants

Income Disparities in Cancer Clinical Trial Enrollment: Evidence and Models for Patient Support

Joseph Unger, Ph.D.

SWOG Statistical Center
Fred Hutchinson Cancer Research Center
Seattle, WA

Conceptual Model: Study to Diffusion of New Cancer Therapy



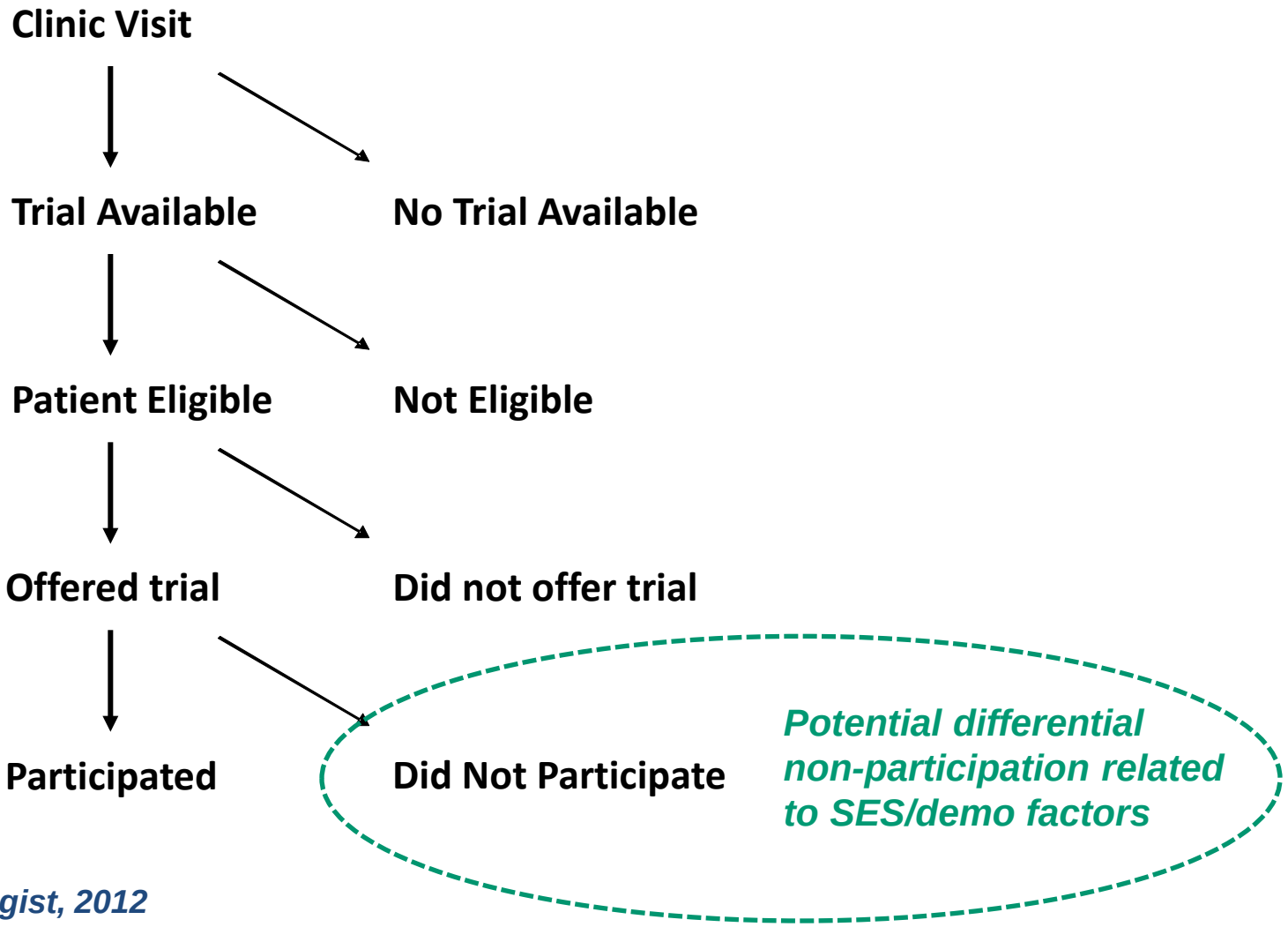
Representativeness

- **Representativeness:** How the characteristics of clinical trial cohort compare to treatment population

- Only 2-3% of adult cancer patients participate in NCI-sponsored clinical trials*

** Murthy, JAMA, 2004; Tejeda, JNCI, 2006*

Conceptual & Study Design Model for Assessing Factors Influencing Clinical Trial Participation



Javid et al, The Oncologist, 2012
Unger et al, JCO, 2013

SES and Clinical Trial Participation

- Clinical trial participation by SES not well studied
- Absence of patient-level SES data in NCI-sponsored trials
- Despite evidence suggesting that SES may be related to both access and outcomes for a range of diseases
  - Whitehall studies (Marmot, Lancet, 1991)
  - Link & Phelan, *Social Conditions as Fundamental Causes of Disease*, 1995

SES and Clinical Trial Participation (cont'd)

- One approach: Use area-level SES estimates from zip code (matched to Census data) as partial surrogate for patient-specific SES
- Useful for statistical adjustment but represents different construct
  - Factors pertaining to neighborhood or regional environment
- Inadequate for examining relationship between SES and trial participation

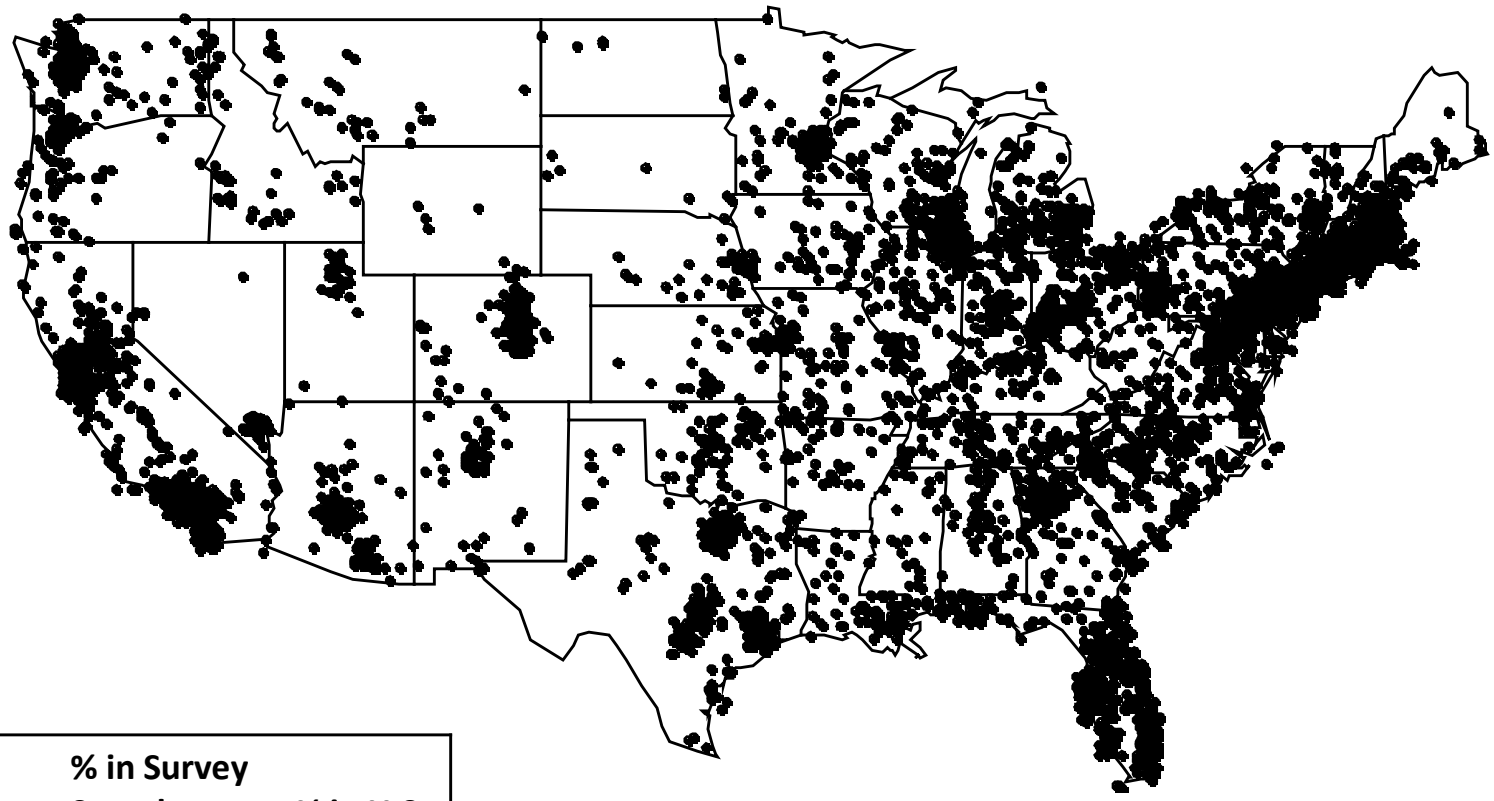
Web Survey Study Design

- Need to reach beyond the usual consortium-sponsored cooperative group data
- Web-based survey study
  - Collaboration with NexCura®, provider of online treatment decision tools for cancer patients
  - Linked to major cancer oriented websites (i.e. American Cancer Society)

Study Design (cont'd)

- Adult patients with new diagnosis of breast, lung, colorectal, or prostate cancer
- Conducted over 4 year period (2007-2011)
- Collected patient level income and education
  - Also age, sex, race, distance to clinic, comorbidity status

Geographic Distribution of Survey Respondents



Region	% in Survey Sample	% in U.S.
West	25%	23%
Midwest	21%	22%
Northeast	19%	18%
South	35%	37%

5,499 patients surveyed
(overall rate = 9.0%)

Regression Results for Income

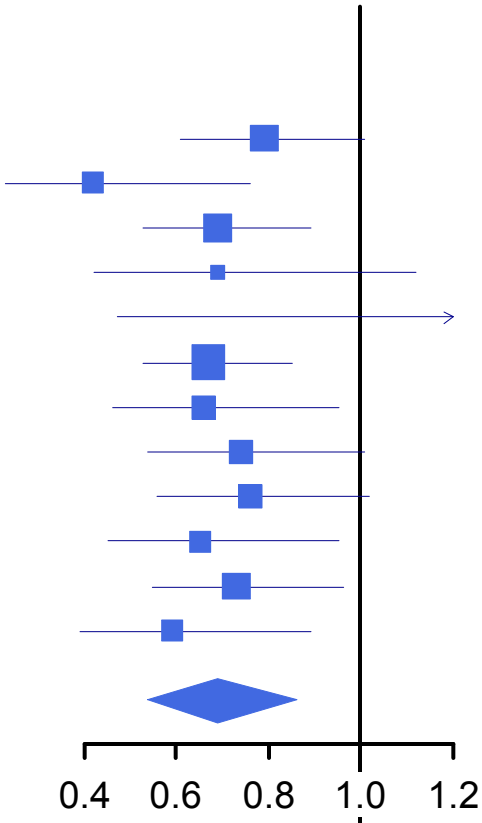
- Income only SES or demographic factor significantly associated with clinical trial participation in multivariable regression
  - Income <$50,000/year, 27% less likely to participate (p=.01)

Cutpoint	% Less Likely	P-value
$20,000	44%	.02
$35,000	27%	.04
$50,000	27%	.01
$100,000	21%	.04

Forest Plot

Association of Income and Clinical Trial Participation by Each Study Factor: Association is Independent of Subgroup Membership

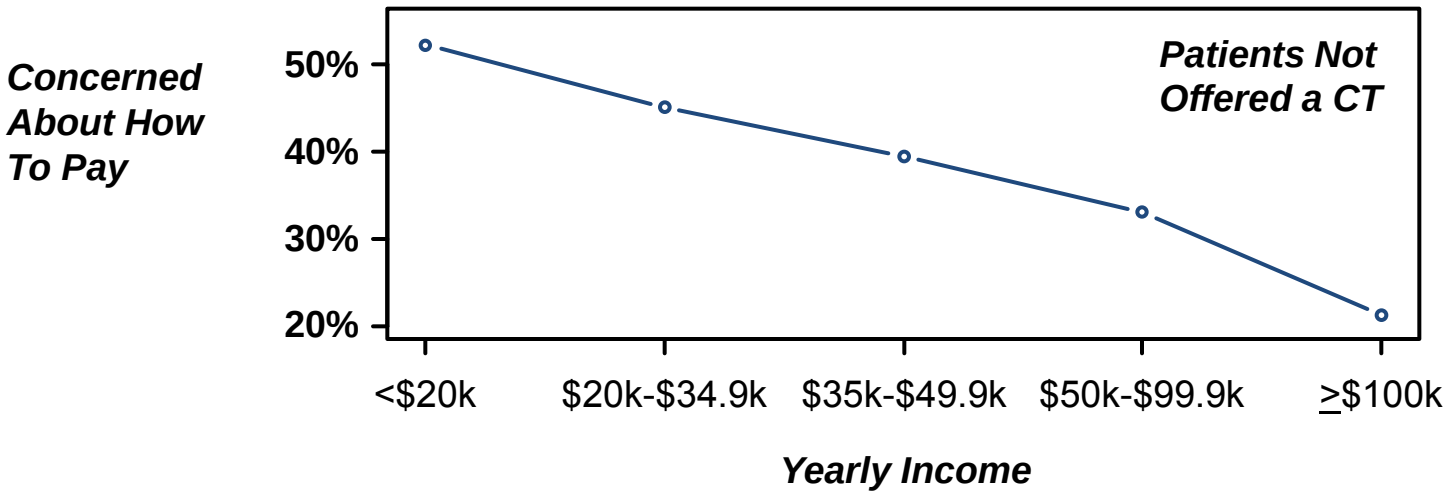
Factor	Category	Sample Size	OR	p-value
Age	≥65 years	954	0.79	.06
	<65 years	3625	0.42	.005
Sex	Female	2832	0.69	.005
	Male	1747	0.69	.13
Race	African American	125	1.51	.49
	White	4454	0.67	.0009
Education	<College	1595	0.66	.02
	≥College	2984	0.74	.06
Comorbidities	0 or 1	2711	0.76	.07
	≥2	1868	0.65	.03
Distance To Clinic	<13 miles	3334	0.73	.03
	≥13 miles	1196	0.59	.01
OVERALL		**4579**	**0.69**	**.001**



Odds of Clinical Trial Participation for Lower Income Patients: Lower Odds ← → Higher Odds

Concern about How to Pay

- Assessed patient attitudes toward CTs
- Lower income patients much more concerned about how to pay for CT treatment (p<.0001)
  - 53% for <$20k/year vs. 24% for >$100k/year



Main Findings

- In multivariate model, lower-income patients much less likely to participate in a clinical trial
- Lower-income patients much more concerned about how to pay for CT participation

Potential Reasons for Income Finding

Is there an insurance effect?

- Consistent finding in subset of patients ≥65 years covered by Medicare

Is there an impact of state laws mandating coverage of clinical trials?

- No evidence that association of income and clinical trial participation differed by type of state (i.e. with vs. without insurance mandate)

Clinical Trial Costs

Are CTs more expensive?

- NCI: Patient care costs for clinical trials are "not appreciably higher" than for non-trial care
- Costs of Cancer Treatment Study (RAND)*
  - Non-significant 6.5% increase for trial patients
  - No increase is prescription out-of-pocket costs**
- But patient cost concerns much higher among lower-income patients

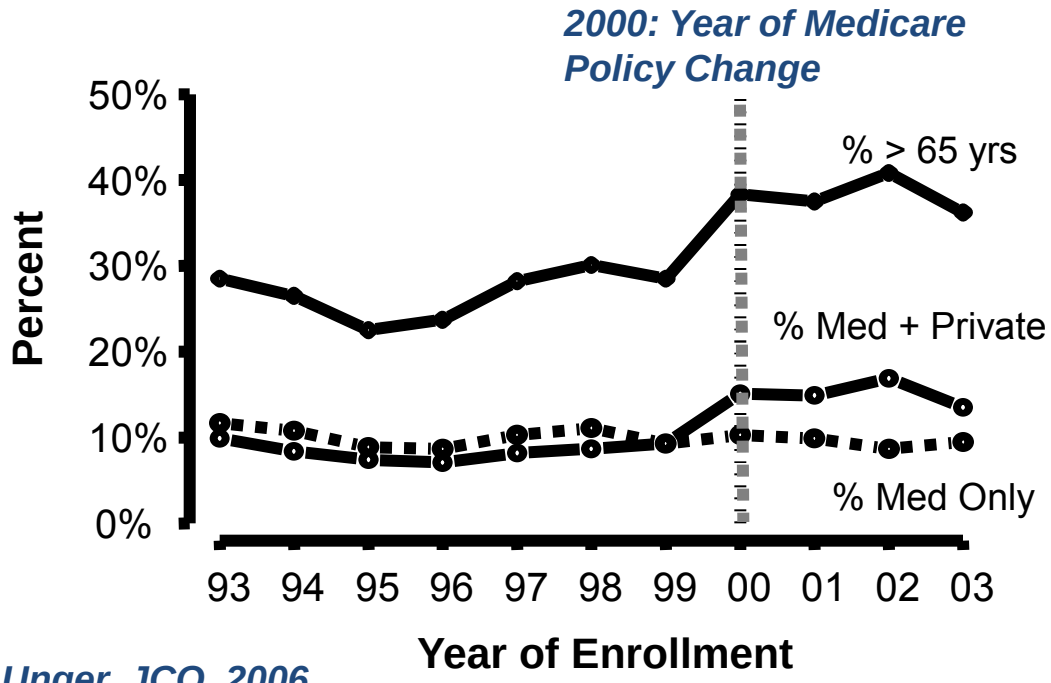
** Goldman, JAMA, 2003*
*** Kilgore, Contemp Clin Trials, 2008*

Clinical Trial Costs (cont'd)

- Concerns about how to pay for treatment in general may interact with anxiety about trial participation to produce a differential impact on lower income patients
- Lower income patients may be more sensitive to:
  - Direct costs (co-pays and co-insurance)
  - Indirect costs (time off work for extra clinic visits)
- Policy Implications: Find ways to help lower-income patients with direct and indirect costs of clinical trial participation

Cover Co-Pays/Co-Insurance

- Cover excess costs for clinical trials for all patients
- Even in an insured population, co-pays and co-insurance deters clinical trial participation*



	'93-'99	'00-'03	P-value
% ≥ 65 yrs	26.5%	38.1%	<.0001
% Med+Private	8.3%	15.2%	<.0001
% Med Only	9.9%	9.7%	.50

** Unger, JCO, 2006*

Payments to Participants

- Pay individuals to participate in NCI-sponsored clinical trials
- In 1900, military surgeon Walter Reed paid subjects $100 in gold to participate in his yellow fever experiments*
- In U.S., the practice of paying patients for trial participation is widespread, but also contentious, highly variable, and lacking in general guidance**

** Lederer, 1995*
*** Grady, 2005*

Payments to Participants (cont'd)

- Careful calibration of size of monetary incentive to avoid "undue influence" per US Common Rule for Protection of Human Subjects
- Concern is that a payment inducement might alter a subject's assessment of potential risks or impair their judgment.
- Little evidence that payment inducements do or do not do this
- See Grady, "Payment of clinical research subjects" (J Clin Invest, 2005)

Policy Prescriptions (cont'd)

- Some worry that payments to patients would produce a disproportionate burden of research on lower income patients
- In contrast, "offering no money… also has the potential to skew the subject pool and contravene distributive justice"*
- Series of tradeoffs and an ethical debate: What are tradeoffs between benefit to society, benefit to individual, and potential harms to individuals

** Grady, 2005*

Payment Models*

- **Market Model:** Market determines how much to pay in order to recruit the number and type of subjects needed in a given time frame
- Based on traditional libertarian theory (supply and demand)
- Higher payments when:
  - Low intrinsic incentive for participation
  - Need to accrue quickly
  - Small eligible patient pool
- Lower payments when high intrinsic incentive for participation

** Dickert & Grady, NEJM, 1999*

Payment Models (cont'd)

- **Wage-payment model:** Payment offered to compensate for time, contribution to study, and effort/discomfort
- Based on egalitarian perspective that participants performing similar functions should be paid similarly
- Amounts to payment based on a standardized hourly wage (i.e. "unskilled" labor rate)
- Completion bonuses to encourage compliance

Dickert & Grady, NEJM, 1999

Payment Models (cont'd)

- **Reimbursement model:** Payment offered to reimburse participants for actual expenses
- Based on egalitarian perspective and the idea that research participation should be revenue neutral for participants (i.e. no financial sacrifice or gain)
- One approach: Reimbursement for travel, meals, parking, etc.
- Alternative: Reimbursement as well for time away from work

Dickert & Grady, NEJM, 1999

Payment Model of Choice*

Wage-payment model

- Greatly reduces the common worry about undue influence
- Standardization among studies will:
  - Contain the cost of research
  - More egalitarian: Does not favor only well funded studies
  - Easier to determine payment
  - Avoids risk-adjusted payments, so encourages risk minimization
- Adheres to “principle of justice”: Treats people serving similar functions similarly

**Dickert & Grady, NEJM, 1999*

Direct to Consumer Advertising

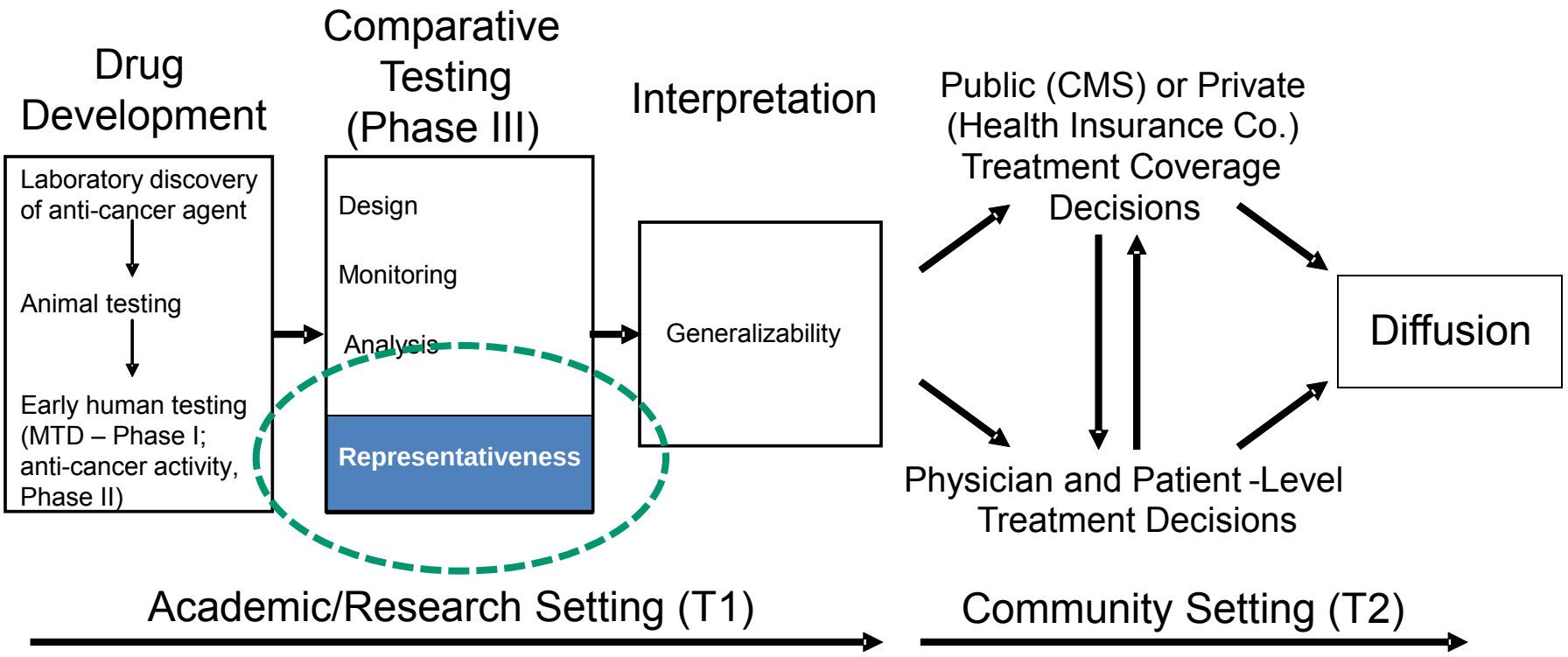
- Direct-to-consumer-advertising (DTCA) targeted in particular to lower income patients
- DTCA has increased in recent years*
- Awareness of oncology-related DTCA is high among cancer patients**

** Donohue, NEJM, 2007*
*** Abel, JCO, 2009*

Conclusion

Why is income representativeness important?

Conceptual Model: Study to Diffusion of New Cancer Therapy



Conclusion

Why is income representativeness important?

- **Feasibility**
  - Better participation of lower income patients could speed the conduct of clinical trials
- **Interpretation**
  - Better participation of lower income patients would better assure the applicability of clinical trial results to all income levels
- **Fairness**
  - Clinical trials offer the newest treatments, so crucial that all income groups have equal access to trials

Thank You