Rapid Case Ascertainment in Population and Hospital-Based Studies: Notes From the Field

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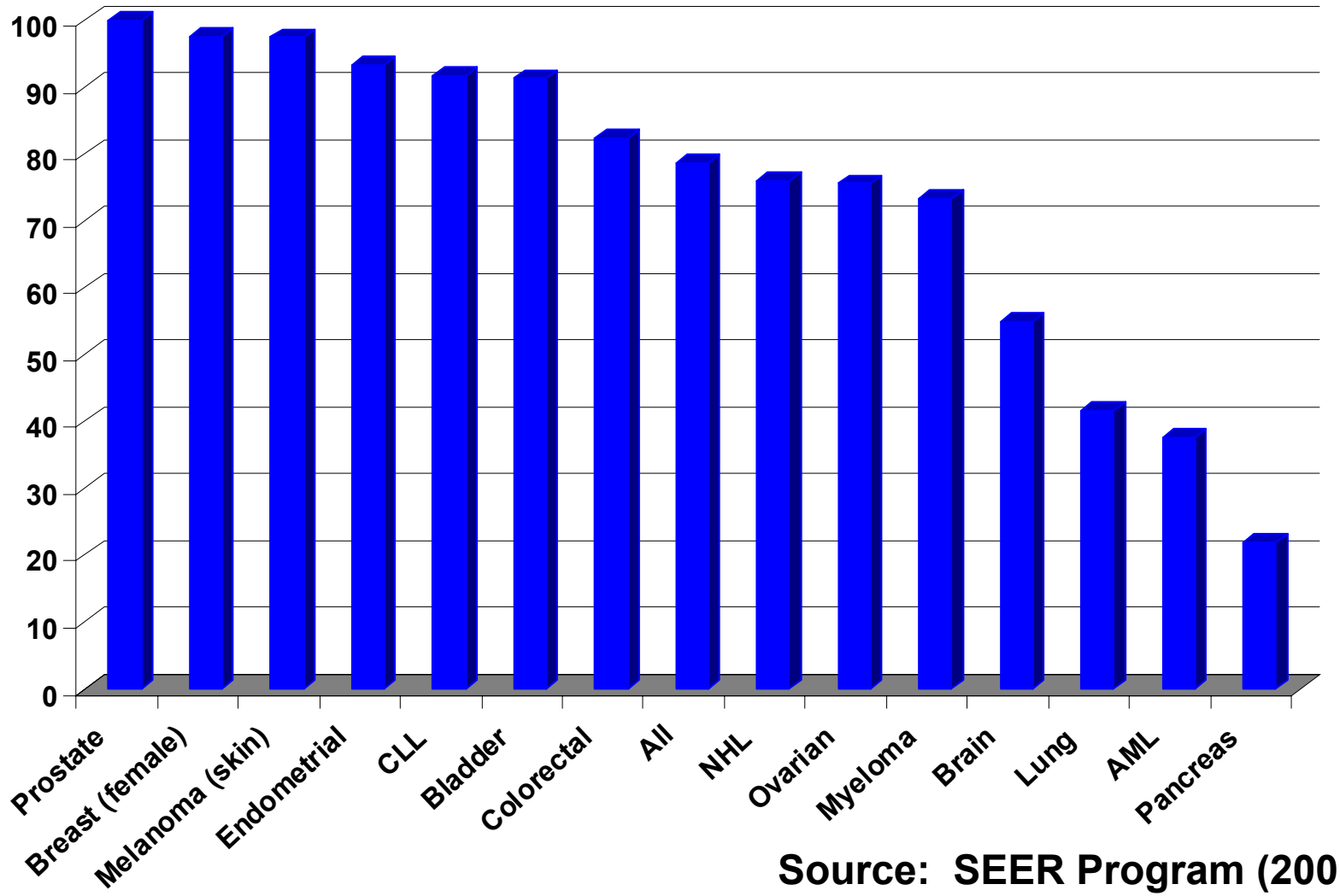
Overview of Presentation

- Why Rapid Report?
- Population-Based Study
  - NCI-SEER Non-Hodgkin Lymphoma Study (1998-2000)
- Clinic-Based Study
  - Mayo Pancreatic Cancer Study

Why Rapid Report?

- **Decrease recall bias**
  - **Ruminate longer to explain cause of disease**
  - **Confuse exposures before/after diagnosis**
  - **Post diagnosis changes could influence recall**
- **Minimize ascertainment bias**
  - **Systematic loss of most aggressive cases of a cancer due to early mortality**

12-Month Survival (1995-2001)

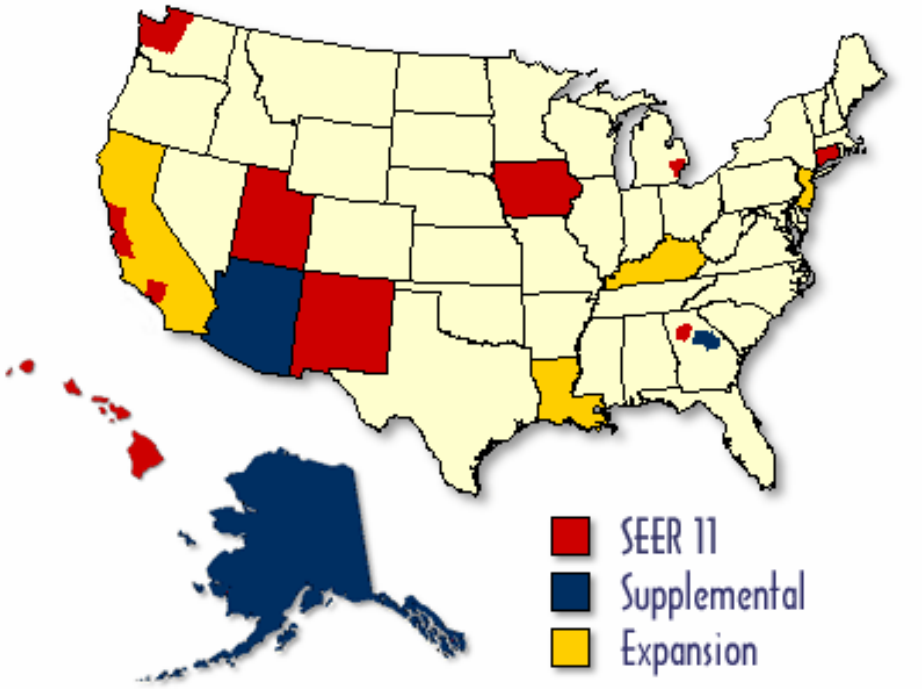


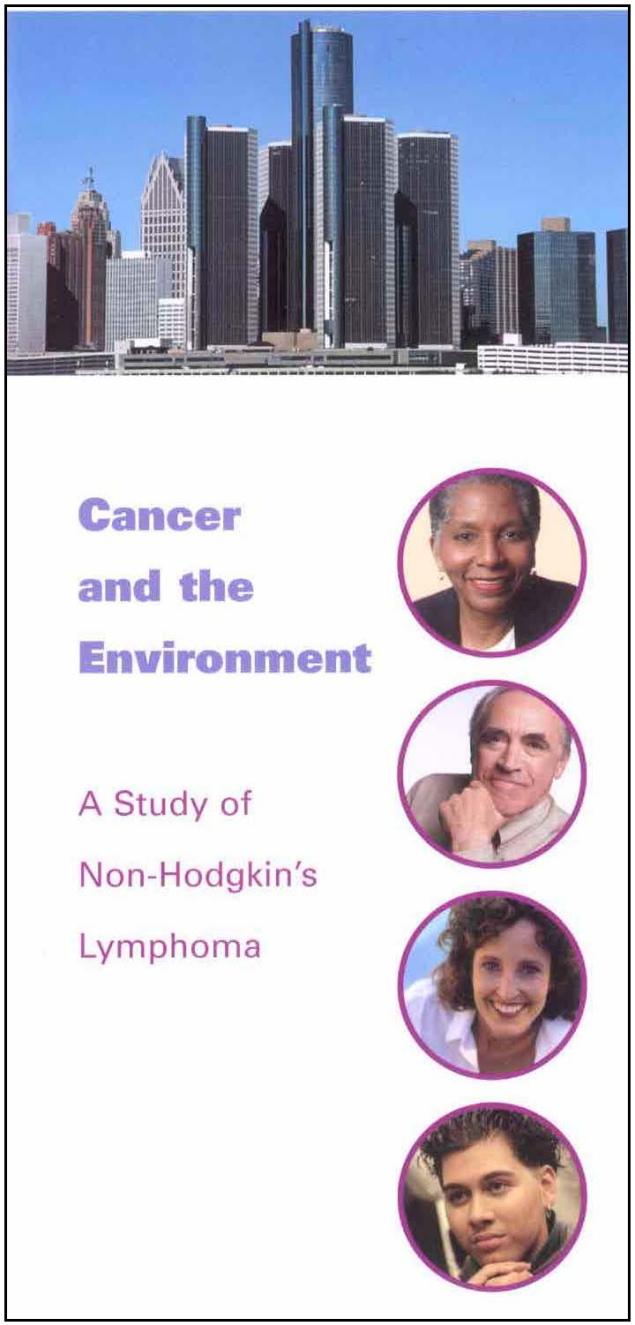
Source: SEER Program (2005)

Approaches to Decrease Bias

- **Include Next-of-Kin Interviews**
  - **Limited exposure assessment of varying validity and reliability**
  - **Best type of control not always clear**
  - **Limited collection of biologic specimens**
    - **Tumor tissue, but often limited for genomic DNA-based studies (and need to have sufficient tissue)**
- **Enroll only living patients**
  - **Enroll before major impact of survival**
  - **Enroll before initiation of therapy**

NCI-SEER Interdisciplinary Case-Control Study of Non-Hodgkin Lymphoma





Goals of the study

- Environmental Risk Factors
  - Household pesticides
  - Occupational exposures (benzene)
- Medical History
- Lifestyle
  - Diet and physical activity
  - Sun exposure
- Biologic specimens
  - DNA: genetic polymorphism studies
  - Serum: Organochlorines; antibodies

Data Collection Scheme

	All	Group A (AA, 50% other)	Group B (all other)
Mail	• Lifetime residence & work calendar	• Family Medical Hx	• Food Frequency Questionnaire • Physical activity
CAPI	• Demographics • Residential pesticides • Occupational history • Hair coloring use	• Detailed medical hx (diseases, surgeries, antibiotics) • Illicit drugs	• Abbrev medical hx • Allergies • Hobbies • Sun exposure • Cell phone
Other	• Consent forms • G.P.S. • Blood (treatment) • Buccal • Dust sample • Water sample		

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In-Person

In-Home Interview

Pre-treatment blood

Case Selection

- **Eligibility**
  - Newly diagnosed July 1998-June 2000
  - Aged 20 to 74 years
  - Uninfected with HIV
- **Sampling scheme**
  - Iowa, Seattle: all cases
  - Detroit, LA: all African-Americans and a random sample of all other
- **Rapid Reporting Systems**

Rapid Reporting - Iowa

- Standard Reporting
  - Begin abstracting 6 mos after diagnosis
  - 15 month lag
- Rapid Reporting
  - Registry field staff increase surveillance
    - Monthly for smaller hospitals/path labs
    - Weekly for larger facilities
  - Report in “early”
    - Laptop electronic form submitted
    - Fax path report to central registry

Iowa Cancer Registry

- Pre-HIPAA
- Temporary Number
  - Not abstracted
- Reconciliation
  - Against Iowa database
    - Is this a recurrence or transformation?
  - Other field reports
    - Concurrent (follow forward)
    - Recent past (follow back)

Iowa Cancer Registry

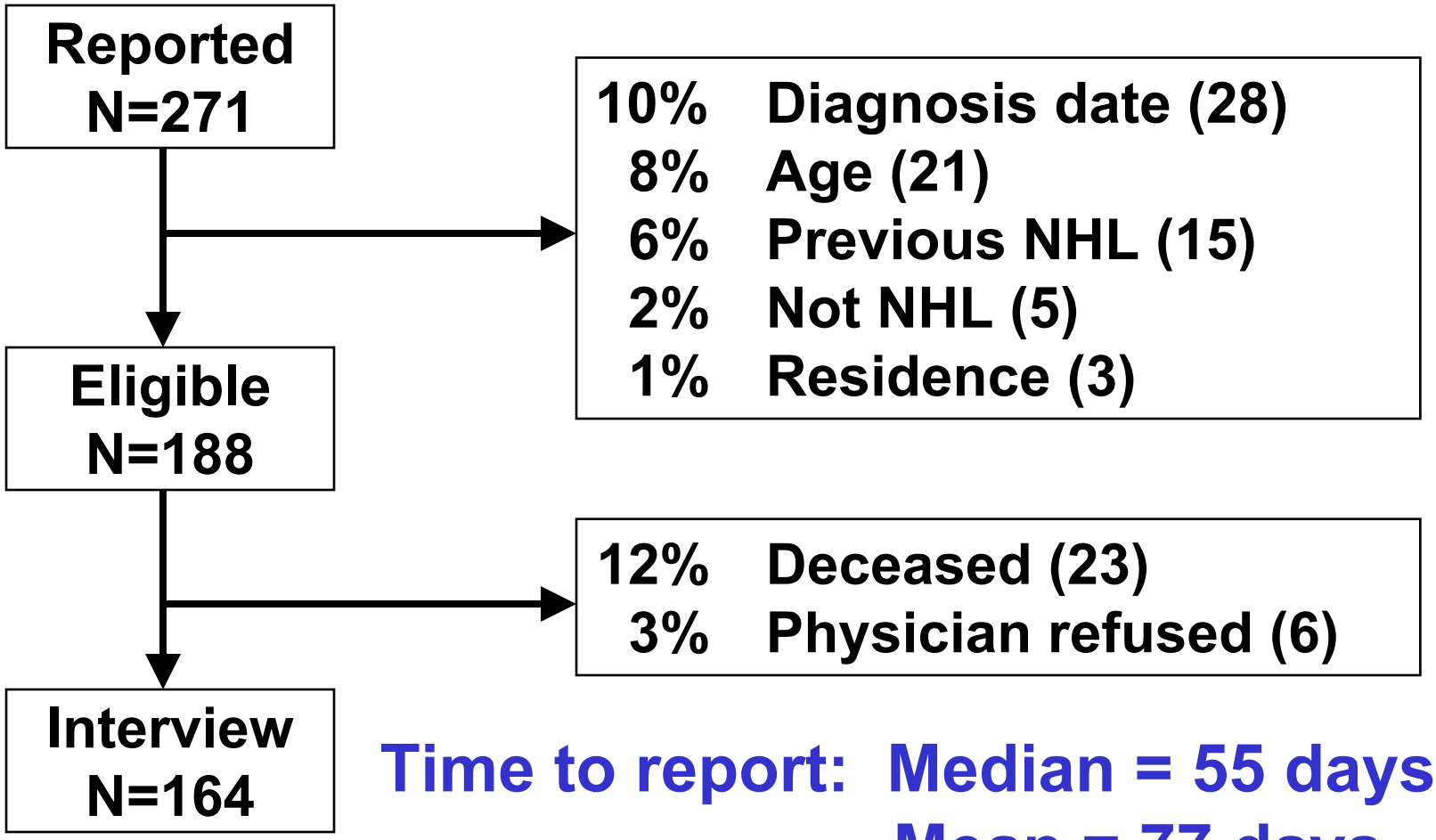
- Check Eligibility (IRB regulated)
  - Date of diagnosis
  - Age at diagnosis
  - Iowa residence
  - Histologically confirmed, new diagnosis of non-Hodgkin lymphoma
    - Chronic Lymphocytic Leukemia
  - (HIV/AIDs status)

Iowa Cancer Registry

- **Passive Consent**
  - **Physician of record (oncologist > family)**
  - **Fax letter and form**
  - **Eligibility criteria**
    - **Asked to report any inaccuracies**
    - **Does patient meet eligibility**
  - **14 days to respond with do not contact**
  - **Letter to cases:**

    "Where your physician's name was available in our database, we have contacted him or her about your participation in this study"

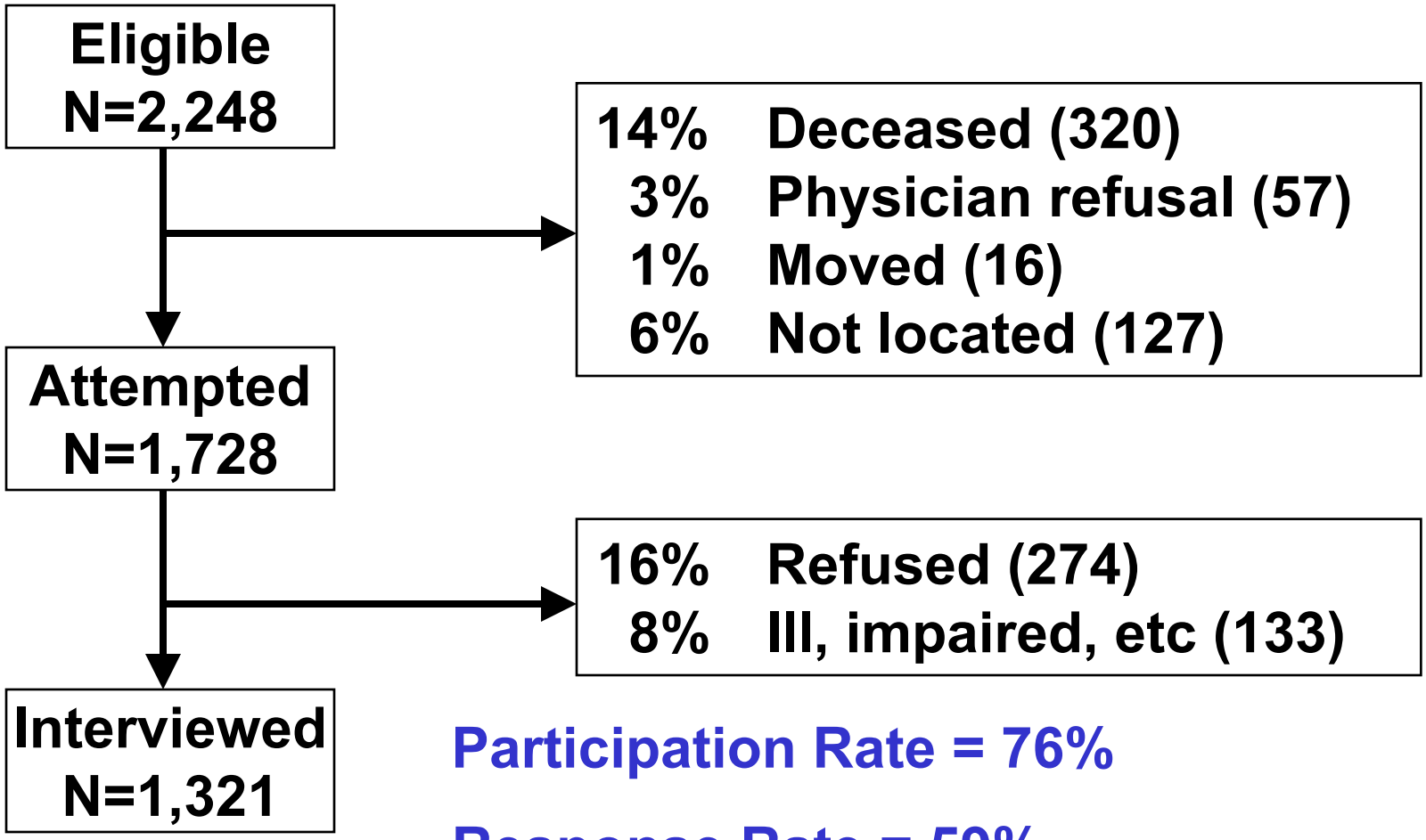
Rapid Reporting
Iowa Experience - First 9 Months



Time to report: Median = 55 days
Mean = 77 days

Results of Full NCI Study

Case Recruitment



Participation Rate = 76%

Response Rate = 59%

Impact of Rapid Reporting

Time from diagnosis to interview	Percent	Cumulative Percent
0 – 3 months	16%	16%
>3 – 6 months	45%	61%
>6 – 12 months	23%	85%
>12 – 24 months	12%	96%
>24 months	4%	100%

Median = 5.0 months, Mean = 7.3 months

NHL Subtype

	Number Inter-viewed	Median Time Dx to Inter-view	Partici-pation rate	Resp-onse Rate	Percent Deceas-ed
All	1321	5.0	76%	59%	14%
SLL	161	4.7	81%	69%	8%
Mantle Cell	50	4.1	78%	66%	10%
Follicular	319	4.6	79%	70%	6%
Marginal Zone	106	5.7	75%	62%	6%
DLBCL	417	4.8	75%	53%	21%
Burkitt	20	5.4	80%	49%	24%
PTCL	20	4.9	77%	43%	42%

Pre-Treatment Blood Specimen

		Untreated		Treated	
	N	%	med	%	med
All	714	18%	3.7	82%	4.6
SLL	98	39%	3.8	61%	4.3
Mantle Cell	33	18%	3.3	82%	3.6
Follicular	191	23%	3.5	77%	4.8
Marginal Zone	65	34%	3.8	66%	5.4
DLBCL	198	3%	5.7	97%	4.5
Burkitt	11	0%	-	100%	6.0
PTCL	29	11%	3.1	89%	4.9

Summary: NHL Study

- **Successful**
  - Shortened time from dx to interview
  - Real time link to physicians
- **Limitations**
  - Ascertainment bias: differential loss of aggressive NHL subtypes
- **Not Successful**
  - Pre-treatment blood
  - Frozen tumor tissue (not a rapid reporting issue on a population basis)

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Impact on Molecular Epidemiology Studies of Pancreatic Cancer

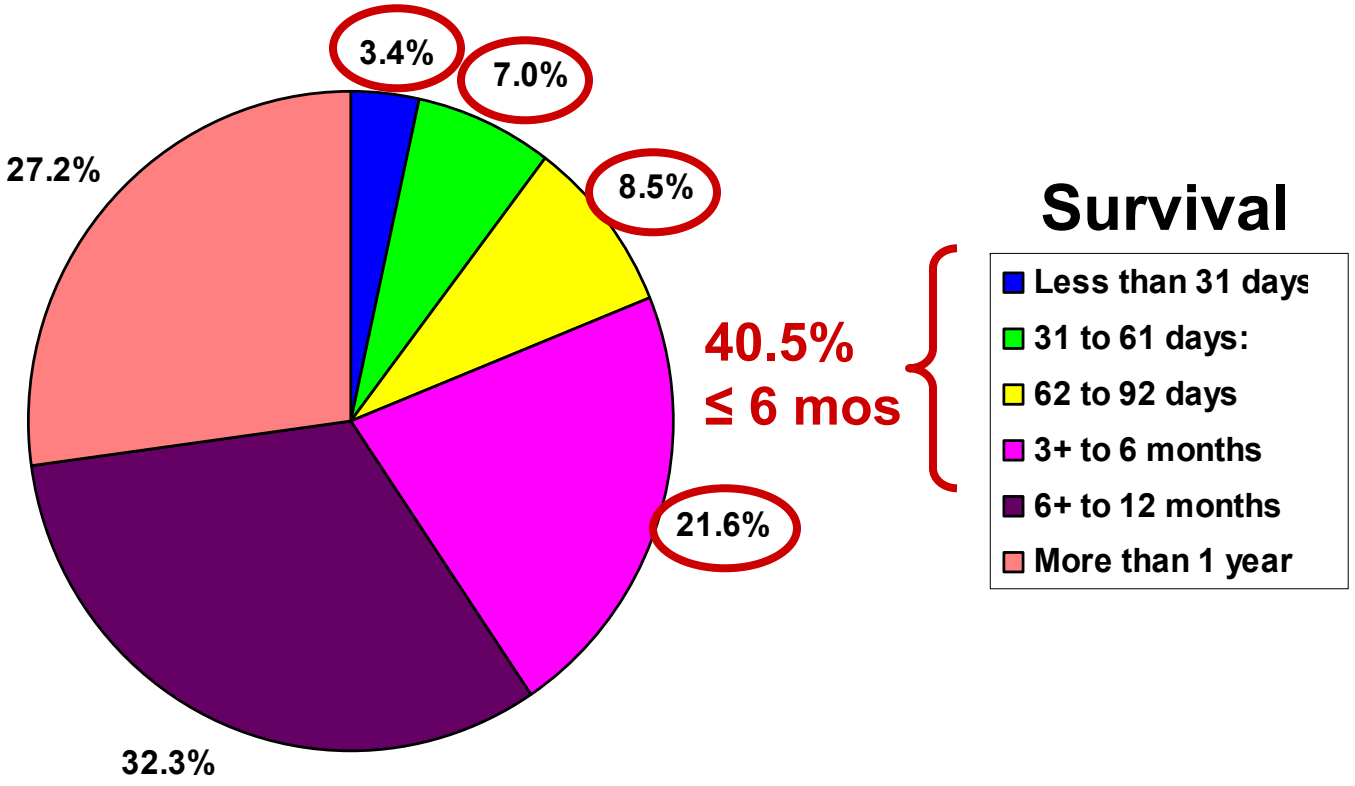
- **Bias related to survival**
  - **Population-based studies of pancreatic cancer – 30-70% deceased and unable to enroll into studies (no DNA)**
- **Bias related to DNA source**
  - **Retrospective, registry-based study in Spain used tumor tissue as DNA source**
  - **Only 34% of 149 cases had useable tumor tissue**

Mayo Clinic Pancreatic Patient Recruitment (G. Petersen, PI)

- Starting in October 2002, all consecutive patients approached
  - At diagnosis (ultra-ultra rapid recruitment)
  - By mail within 2 months (ultra-rapid recruitment)
- HIPAA (Preparatory to Research)
- Over 600 patients enrolled to date
  - 92% within 30 days of diagnosis
  - 80% consent rate

Bias By Survival

Deaths among 412 recruited subjects, Mayo Clinic Pancreatic Cancer Registry



Pilot Study Results
Allele/Genotype Frequencies

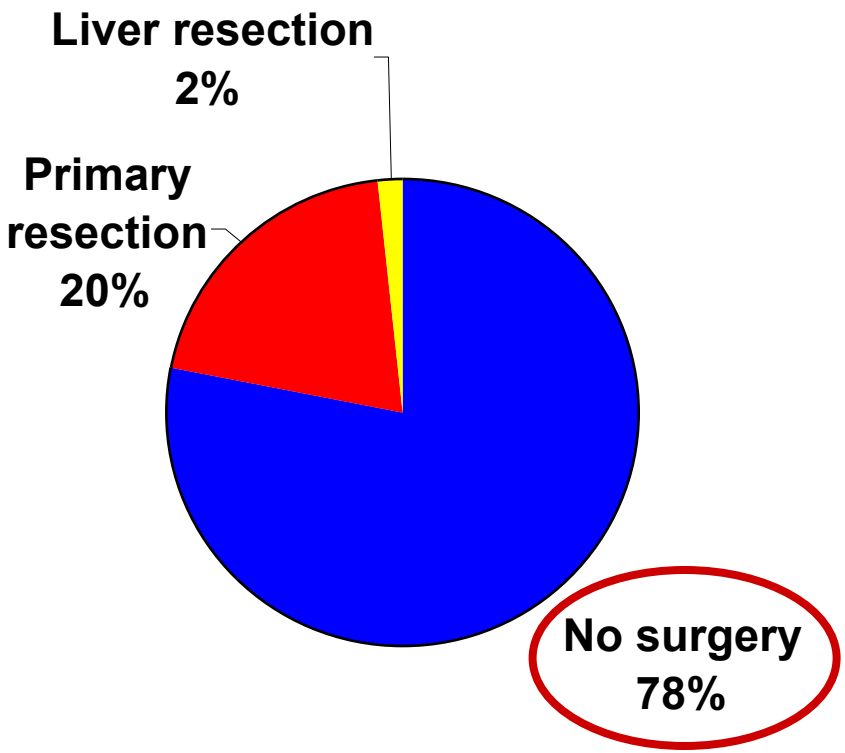
Candidate Genes	Controls (N=62)	Cases		
		All (N=62)	Short (N=31)	Long (N=31)
CYP2E1 / G1293C / (C)	0.02	0.02	0.02	0.02
CYP2E1 / C1053T / (C)	0.97	0.98	0.98	0.98
GSTT1 / (Null)	0.18	0.15	0.16	0.13
GSTM1/ (Null)	0.53	0.48	0.45	0.52
NQO1 / (C)	0.78	0.88	0.82	0.95

Short: died within 4 months of diagnosis
Long: survival >9 months

Source: Petersen GM, et al. (unpublished)

Bias By Tumor DNA Availability

Surgery among 412 recruited subjects, Mayo Clinic Pancreatic Cancer Registry



Pilot Study Results
Allele/Genotype Frequencies

Candidate Genes	Controls (N=61)	Cases		
		All (N=62)	No Surgery (N=52)	Surgery (N=10)
CYP2E1 / G1293C / (C)	0.02	0.02	0.01	--
CYP2E1 / C1053T / (C)	0.97	0.98	0.98	1.00
GSTT1 / (Null)	0.18	0.15	0.15	0.10
GSTM1/ (Null)	0.53	0.48	0.46	0.60
NQO1 / (C)	0.78	0.88	0.87	0.94

Source: Petersen GM, et al. (unpublished)

Conclusions

- **Rapid reporting critical for identifying cases quickly**
  - **Decrease ascertainment bias related to survival**
  - **Increase the percentage of cases with biologic specimens**
- **For some cancers, ultra-rapid reporting through hospital-based registries may be required**

Acknowledgements

NHL Case-Control Study

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Pancreatic Cancer Study

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