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& Population Sciences

# *Issues in Epidemiologic Studies of Gene-Environment Interactions*

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Sciences**

**National Cancer Institute  
National Institutes of Health**



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*Joseph Fraumeni, M.D., Cancer and the Environment, Institute of Medicine, 2002*

**“The big challenge for epidemiology now is to develop strategies to ensure that the advances in human genomics are incorporated appropriately into population studies, as well as family-based, and hybrid studies.”**



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## Importance of “low-risk, low-penetrance” genes

- ▶ “Why have we failed to find the low penetrance genetic constituents of common cancers?” Neil E. Caporaso, *CEBP*; 11:1544-49, 2002.
- ▶ “Gene-environment interaction and aetiology of cancer: what does it mean and how can we measure it?” Paul Brennan, *Carcinogenesis*; 23:381-7, 2002.



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# Large Scale Biomedical Science



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# Large Scale Biomedical Science

- ✓ Broad goals
- ✓ Long range strategic planning
- ✓ Higher total costs
- ✓ Lower per-patient costs
- ✓ Requires complex management
- ✓ Interdisciplinary
- ✓ Develops resource infrastructure



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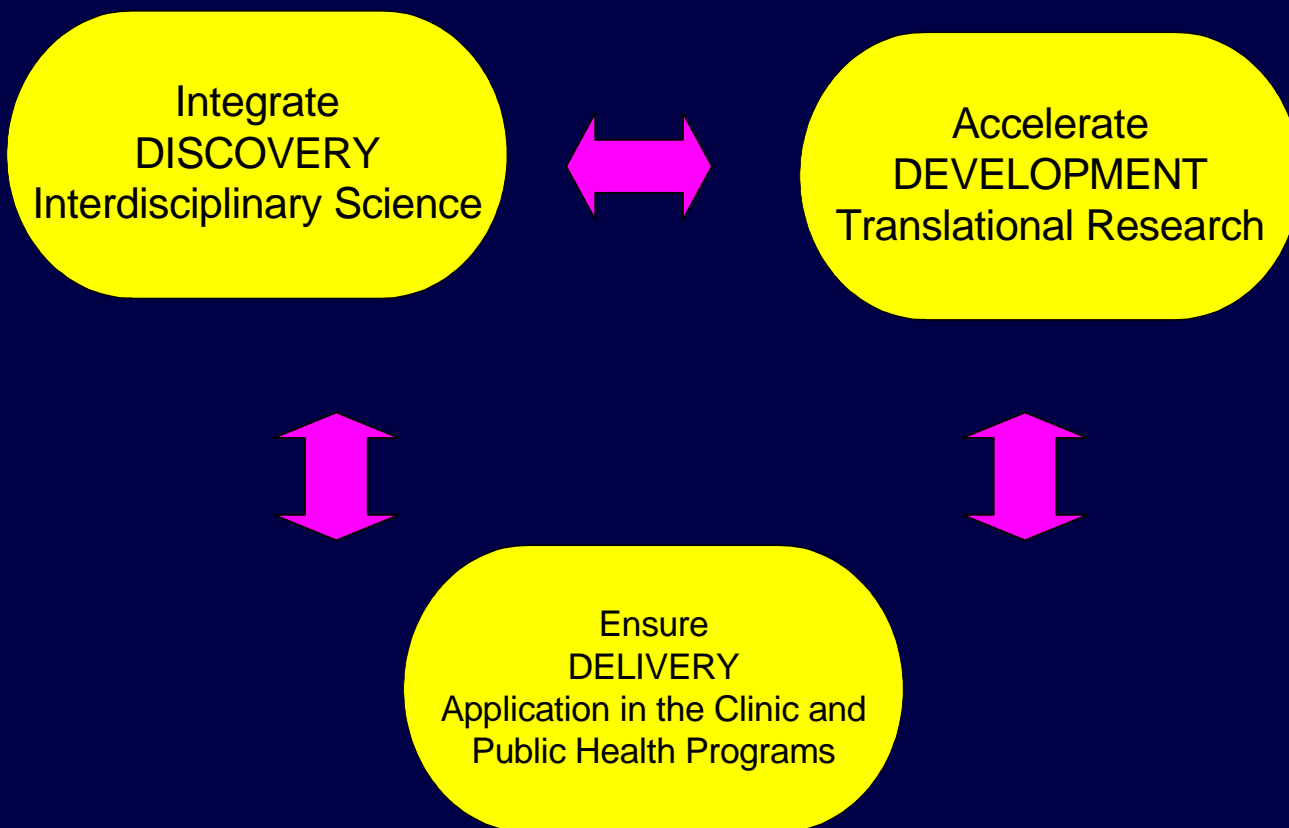
# The Devil is Always in the Details





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# Goals of NCI: Eliminate Suffering and Death by 2015





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**NCI's Bold New Initiatives Include...**

**Molecular Epidemiology!**

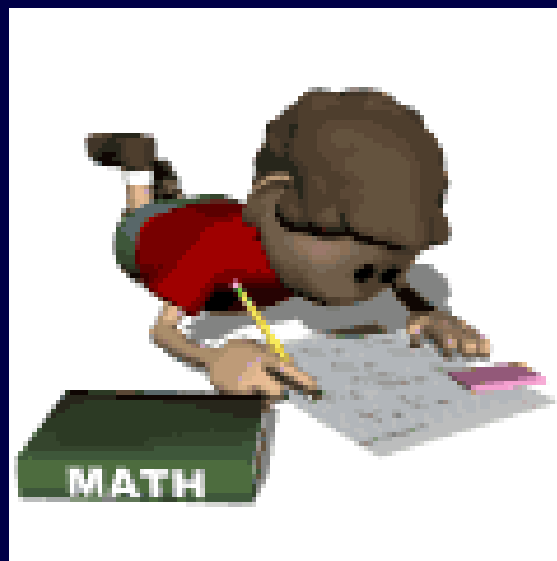




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# Observations from a Program Perspective





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# Areas to Consider

- **Big Science = Big Budgets**
- **A Multitude of Funding Mechanisms**
- **Data Sharing**



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Payline / > \$1M Costs / Average \$T2

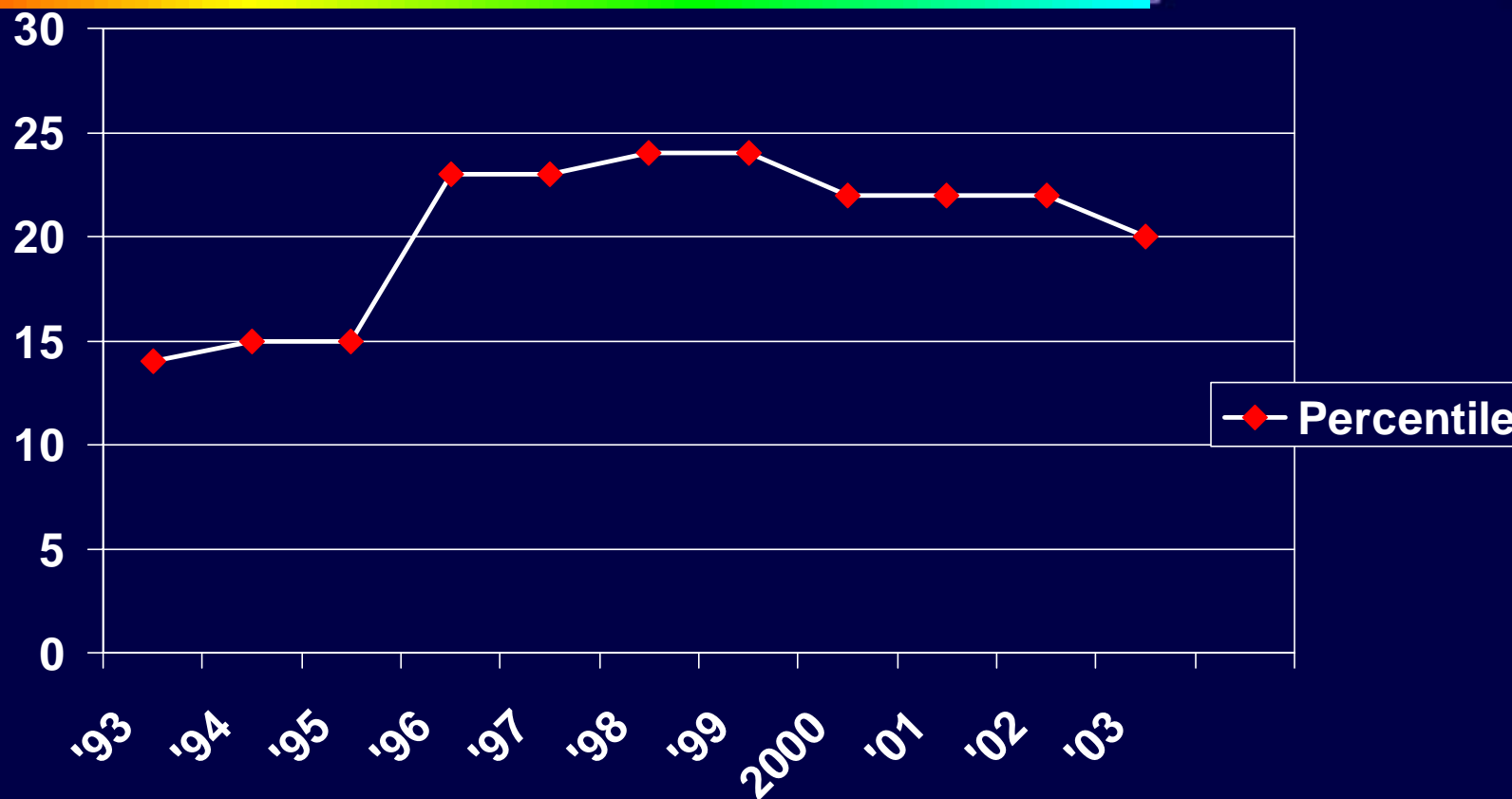
**Big Science =**

**Big Budgets...**



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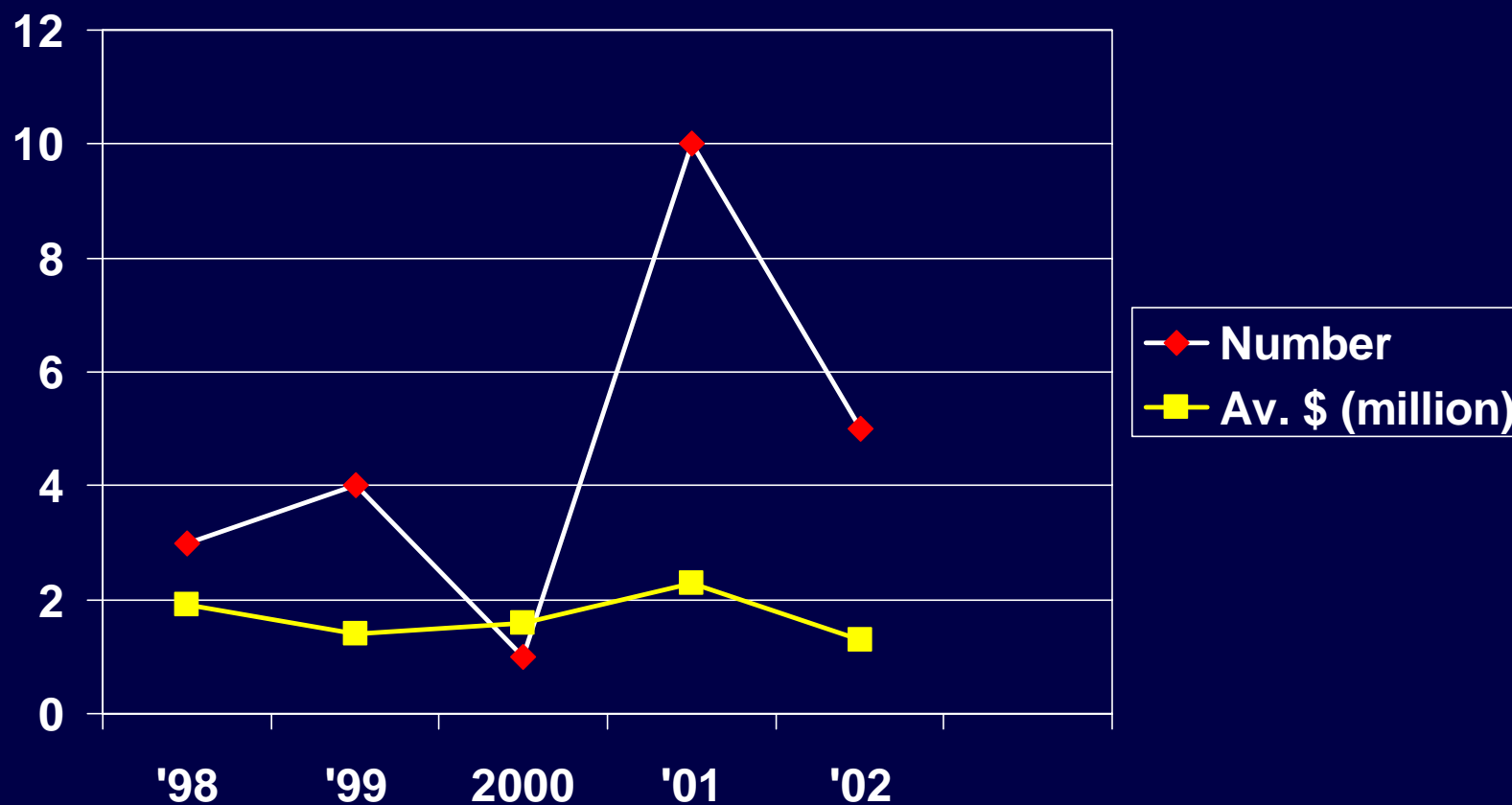
# R01 Paylines at the NCI





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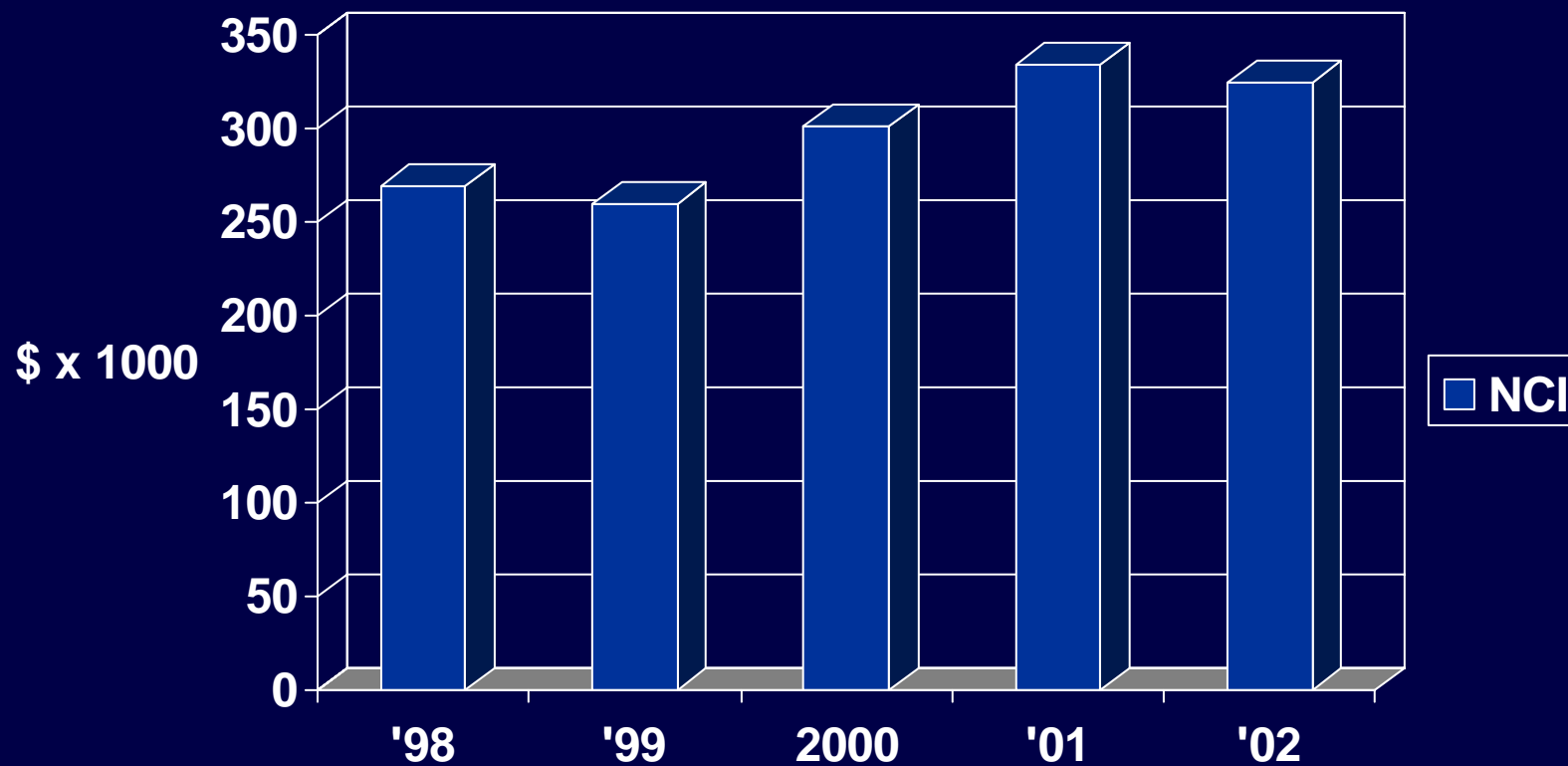
# NCI R01s Over \$1 Million Direct Costs Per Year





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# R01 Average Cost, Competing





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R01 / U01 / R03 / N01 / P01

# A Multitude of Funding Mechanisms



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# Investigator-Initiated (R01)

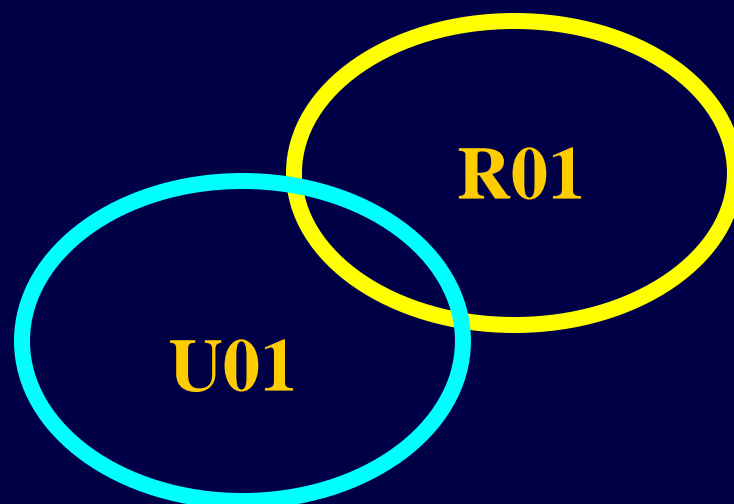
**R01**





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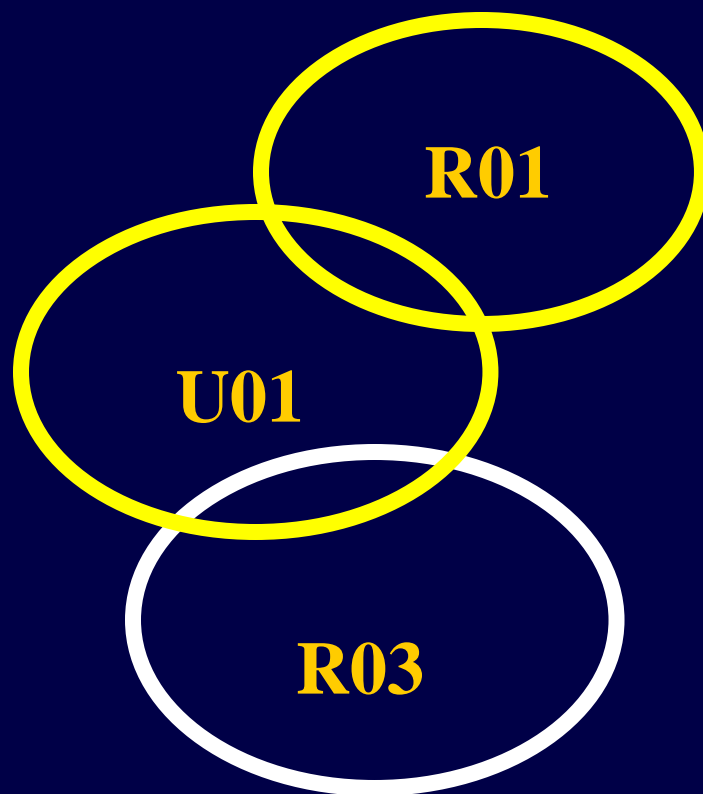
# Cooperative Agreement (U01)





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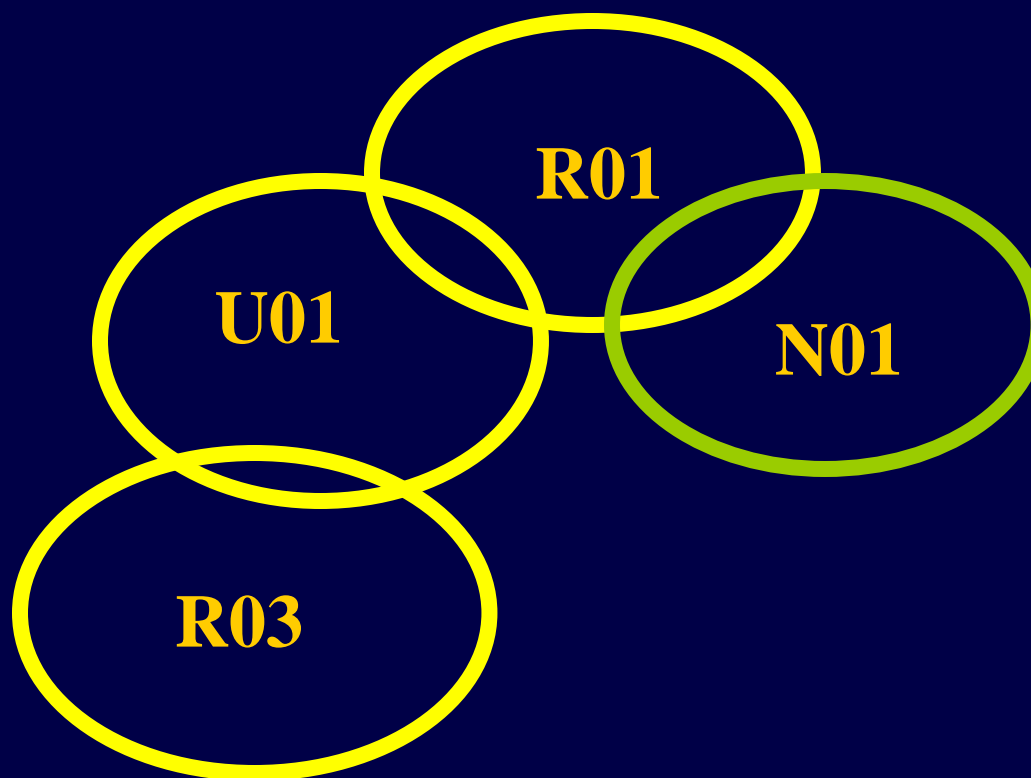
# Small Grant (R03)





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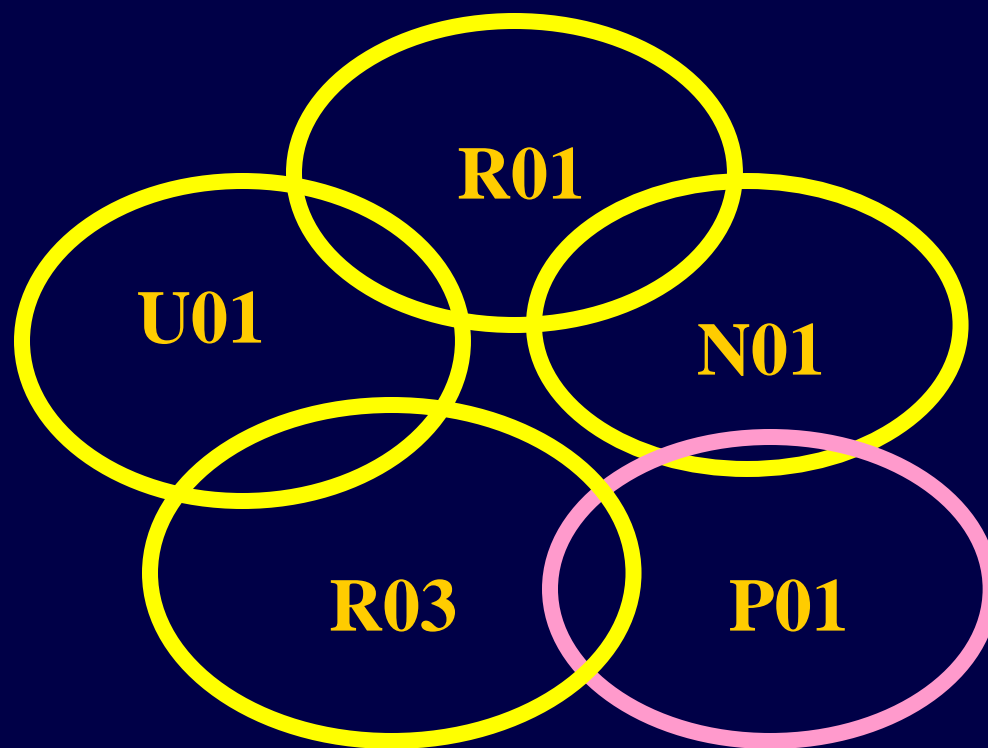
# Contract (N01)





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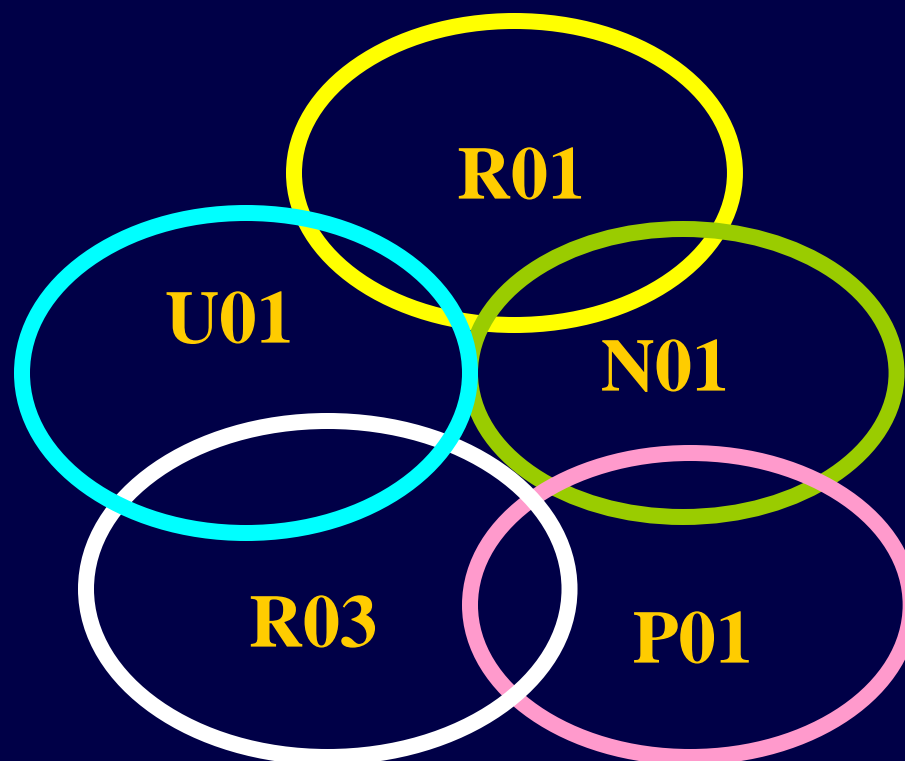
# Program Project (P01)





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# Making Them Work Together





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# Cohorts in the Consortium

Study	Year started	Subjects with blood samples	Breast cancer cases	Prostate cancer cases
-EPIC	1992	397,256	2,050	900
-ACS (CPS-II)	1998	39,000	500	1,450
-ATBC	1991	20,500	-	1,180
HARVARD (4)				
-Physicians HS	1982	20,000	-	1,500
-Nurses HS	1989	32,826	945	-
- HealthProfS	1993	33,240	-	600
OTHER				
- WomenH	1993	28,263	675	-
-MultiEthnicC	1983	100,000	1,990	2,400
-PLCO	1993	75,000	-	1,000
<b>Total</b>		<b>746,085</b>	<b>6,160</b>	<b>9,030</b>



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Why / Who / What / When / How

# Data Sharing



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# NIH Viewpoint on Data Sharing

**“Data should be made as widely and freely available as possible while safeguarding the privacy of participants, and protecting confidential and proprietary data.”**

***--Final NIH Statement on Sharing  
Research Data, February 26, 2003***





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## Effective 10/01/2003.....

- ▶ NIH *expects* timely release and sharing of final research data for use by other researchers.
- ▶ NIH *expects* applications to include a plan for data sharing, or state why it is not possible, if study is  $\geq$ \$500k in any study year.
- ▶ The policy applies to all contractors.



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## To Whom Does the Policy Apply?

- ▶ **Intramural scientists**
- ▶ **Extramural scientists seeking grants, cooperative agreements, and/or contracts**
- ▶ **Graduate students and fellows**



## What is Meant by “Data?”

- ▶ **Final research data necessary to validate research findings**
- ▶ **Does not include:**
  - ▶▶ **Partial datasets or preliminary analyses**
  - ▶▶ **Drafts of scientific papers**
  - ▶▶ **Internal communications**
  - ▶▶ **Software programs or algorithms**



## What is Meant by Data, cont?

- ▶ **Especially important:**
  - ▶▶ **unique datasets that cannot be replicated easily, if at all**
  - ▶▶ **large, expensive datasets**



## What is Meant by “Timely?”

- ▶▶ **“First and continuing use, but not prolonged exclusive use”**
- ▶▶ **Usually no later than the acceptance for publication of the main findings from the final dataset**
- ▶▶ **“Investigators who collected the data have a legitimate interest in benefiting from their investment of time and effort”**



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## How to Share Data

- ▶▶ **Place in public archives**
- ▶▶ **Place in restricted access data centers**
- ▶▶ **Provide in publications**
- ▶▶ **NIH will provide support for this if PI includes costs in budget and budget justification**



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## Assessment of the Data Sharing Plan

- ▶ **The plan is not assessed during peer review beyond assuring that it is present.**
- ▶ **The assurance is made by program staff.**



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<http://epi.grants.nci.nih.gov>

