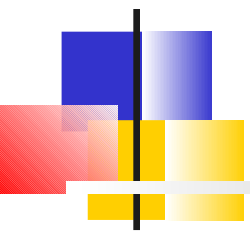


# **Shanghai Women's Health Study**

## **A Unique Population Laboratory for Epidemiologic Research**



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# Why Conduct Cancer Epidemiology Studies in China?

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- ~25% of the world's population
- Asian Americans - a rapidly growing population in the United States
- Unique patterns of cancer occurrence and lifestyle and environmental exposures
- No apparent genetic admixture
- Enhanced study methodology and feasibility
- Populations accessible for research, with large numbers of eligible participants
- Opportunity to evaluate the consistency of study



# Shanghai Women's Health Study

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- Funded by NCI and initiated in 1996 - **“Cancer risk reduction and diet – A cohort study of women”**
- To recruit 75,000 Chinese women in Shanghai for long-term epidemiological studies of cancer and other chronic diseases
- To collect biological samples to evaluate biomarkers
- Zheng W et al. Am J Epidemiol 162:1123-31, 2005



## Response rates at baseline recruitment

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	N	%
Interviewed	75,221	92.7
Specimen collected		
Blood	56,831	75.8
Urine	65,754	88.4
Buccal cells	8,934	49.3

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Zheng W et al, Am J Epidemiol (2005)

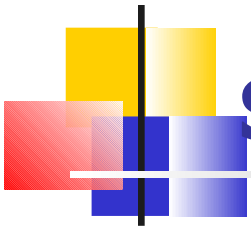


## Large-Scale Cohort Studies Directed by Vanderbilt Investigators

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Study (YR initiated)	Cohort Size	Biological Specimens		
		Blood	Urine	
Buccal Shanghai Women (1996)	75,000	56,800	65,800	8,900
Shanghai Men (2000)	61,600	46,200	54,700	8,600
US Southern Cohort (2001)*	90,000	40,000	23,000	41,000
<b>Total</b>	<b>226,600</b>	<b>143,000</b>	<b>143,500</b>	<b>58,500</b>

\*Subject recruitment is underway and numbers are projected.



## SWHS Active Follow-up Scheme

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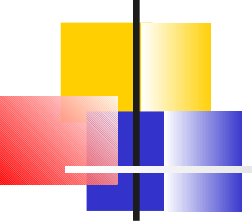
Survey (year)	Response rate (%)	Exposure assessment
1 <sup>st</sup> Follow-up (2000-02)	99.8/ 91.0 (FFQ)	FFQ, Pulse, BP, PA, tea, environmental tobacco smoke
2 <sup>nd</sup> Follow-up (2002-04)	98.7	Occupational history, night-shift work, asthma screening
3 <sup>rd</sup> Follow-up (2004-07)	~96.5	Sleep habits, PA, family history of CHD/diabetes/ cancer, weight, BP, pulse, husband's outcomes, asthma screening
4 <sup>th</sup> Follow-up (2007-10)	N/A	FFQ, diabetes, BP, Pulse, weight, sleep habits, depression, oral hygiene, HRT, Chinese medicine, asthma screening



## Examples of Recent Research Findings

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- Novel Genetic susceptibility locus for breast cancer
- Urinary PGEM level and colorectal cancer risk
- Usual soy food intake and selected health outcomes



## Association of rs2046210 with breast cancer risk: Results from the Shanghai GWAS

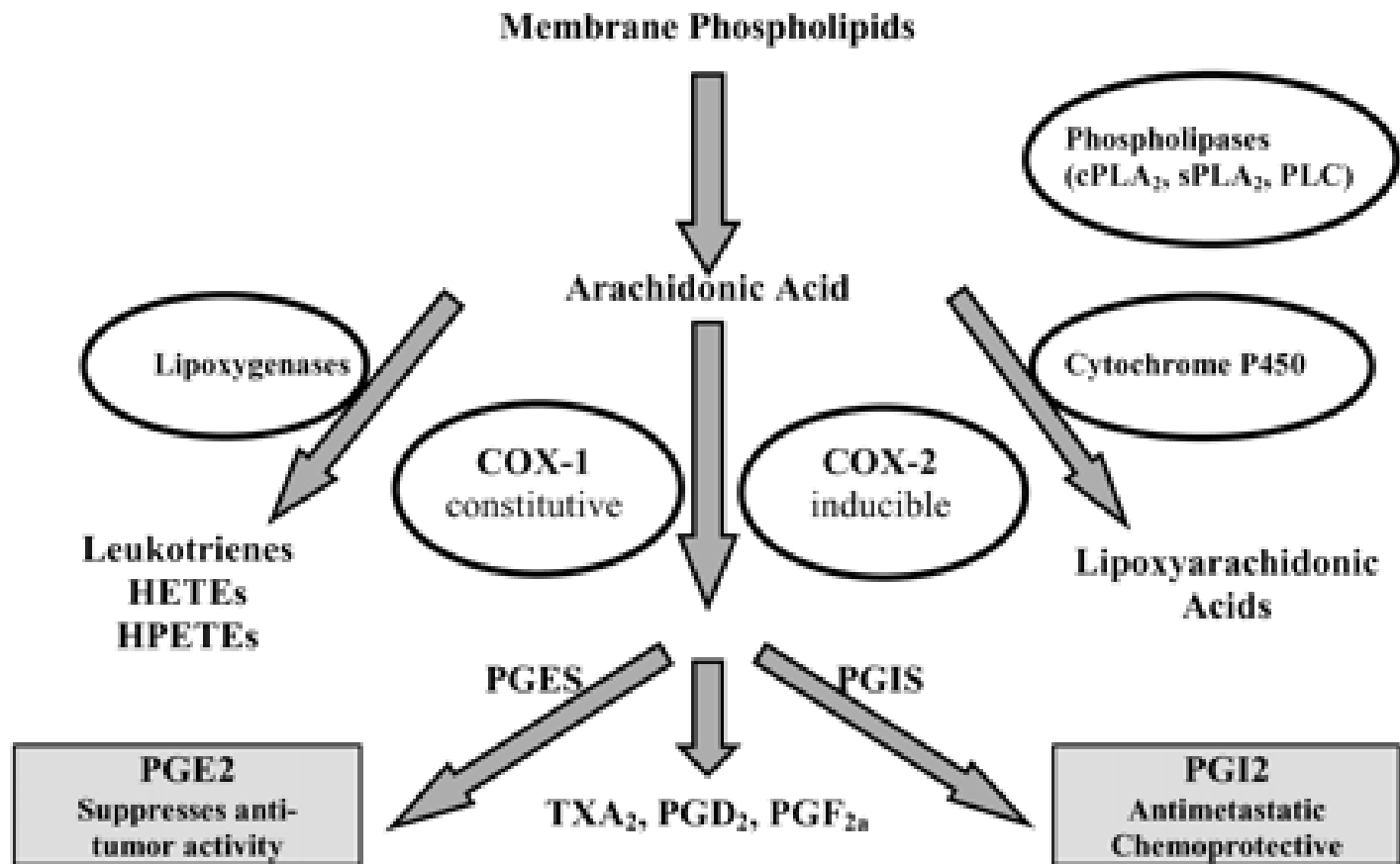
	Cases/ controls	OR <sub>het</sub> (95% CI)	OR <sub>hom</sub> (95% CI)	P for trend
Discovery*	1505/1522	1.30 (1.12-1.52)	1.56 (1.26-1.94)	1.4x10 <sup>-5</sup>
Replication I*	1554/1576	1.22 (1.04-1.42)	1.57 (1.26-1.96)	3.9x10 <sup>-5</sup>
Replication II*	3472/900	1.59 (1.35-1.87)	1.56 (1.25-1.96)	3.3x10 <sup>-7</sup>
Pooled §	6472/3962	1.36 (1.24-1.49)	1.59 (1.40-1.81)	2.0x10 <sup>-15</sup>

\*Adjusted for age and education  
(2009)

§ Adjusted for age, education, stage, and other risk factors

Zheng W et al. *Nature Genetics*

# COX-2, PTGES, PTGIS





## Urinary PGE-M level and colorectal cancer risk

	Urinary PGE-M (by quartiles)				P for trend
	Q <sub>1</sub>	Q <sub>2</sub>	Q <sub>3</sub>	Q <sub>4</sub>	
Colon/rectum	1.0	2.5*	4.5*	5.6*	<0.001
Colon	1.0	2.1	4.8*	4.9*	0.002
Rectum	1.0	3.1	4.1	7.2*	0.008

\* P<0.05

Cai Q et al, J Clin Oncol (2006)



# Association of usual soy food intake and selected health outcomes

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- Breast cancer risk (Am J Clin Nutr, 2009)
- Colorectal cancer risk (Am J Clin Nutr, 2009)
- Coronary heart disease risk (J Nutr, 2003)
- Bone fracture risk (Arch Intern Med, 2005)
- Blood pressure (Am J Clin Nutr, 2005)
- Type 2 diabetes (Am J Clin Nutr, 2007)



# Major biological effects of soy isoflavones

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- Weak estrogenic or anti-estrogenic effects
  - Compete with  $E_2$ ,  $\downarrow$   $E_2$  synthesis,  $\uparrow$  SHBG synthesis
- Inhibition of tumor cell growth and proliferation
- Effects on cardiovascular health
  - $\downarrow$  BP,  $\downarrow$  LDL,  $\uparrow$  vascular reactivity,  
 $\downarrow$  thrombus formation
- Effects on bone health
  - $\downarrow$  bone resorption,  $\uparrow$  bone formation,  $\uparrow$  IGF-1,  
 $\uparrow$  BMD
- Improve insulin sensitivity



# Challenges in observational studies of soyfood intake and health outcomes

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## United States

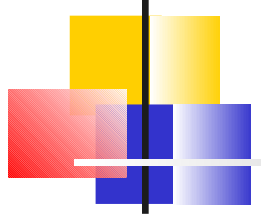
- Historically low intake
  - Barriers for informative analyses
  - Possible selection bias
- Distributed in a wide range of foods
  - Difficult to assess intake levels
  - Possible confounding by other dietary factors

## China

- High intake with sufficient between-person variation
- Commonly consumed in a small range of food items
  - Relatively easy to assess intake level accurately
    - FFQ vs multiple 24-HDR :  $r = 0.49$
  - FFQ vs multiple urinary isoflavonoid measurements:  $r = 0.48$
  - Multiple urinary isoflavonoid measurements :  $ICC = 0.36 - 0.68$

# Risk of breast cancer by usual soy isoflavone intake

## Shanghai Women's Health Study



	Intake level (by quintile)					P for trend
	1 (low)	2	3	4	5	
All women	1.00	0.87	1.02	0.77*	0.81	0.09
Premenopausal	1.00	0.66	0.80	0.48*	0.44*	<0.001
Postmenopausal	1.00	1.05	1.22	1.00	1.09	0.80

\* P < 0.05

Lee et al., Am J Clin Nutr (2009)



# Soyfood intake and colorectal cancer risk by menopausal status and anatomic site

## Intake level

	Low	Middle	High	P for trend
Menopausal Status				
Pre-	1.00	0.84	1.17	0.62
Post-	1.00	0.86	0.61*	0.003
Combined	1.00	0.86	0.67*	0.008

\* $P \leq 0.05$

Yang G et al, Am J Clin Nutr (2009)



## Challenge - How to balance science and logistics?

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- Obtaining/maintaining high quality exposure/ follow-up data and biological samples
- Publishing study results/participating in consortium projects at the right time
- Dealing with issues related to study feasibility, funding, and manpower



# Challenges in International Epidemiology Studies

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- Study protocols & instruments are often unavailable
- Language/cultural barriers may hinder research implementation
- Existing infrastructure may be inadequate
- Availability of well-trained researchers may be limited
- Remote study sites add complexity to research coordination
- Changes in government policies could affect research operations



# SWHS's Contribution to Consortia

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- Pooled analyses of dietary factors for cancer (2005- )
- GWAS of pancreatic cancer (PanScan, 2007-)
- Blood vitamin D & rare cancer risk (VDPP, 2007-)
- BMI and total mortality (ACC/BMI, 2008- )
- Asia Breast Cancer Consortium (2008-)
- GWAS of stomach cancer (2009 - )
- Inflammation/Vit D & endometrial cancer risk (planned)
- Diet/gene & upper GI cancer (Planned)
- Sex hormones & ovarian cancer (Planned)
- Biomarkers & ovarian cancer (Planned)
- Pooled analyses of lymphoma risk factors (Planned)
- Fine-mapping of breast cancer susceptibility loci (Planned)
- Asia Cohort Consortium – multiple projects (discussed)
- Others .....



# Lessons Learned from Working on Consortium Projects

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- Choose appropriate projects
- Develop simple, well-defined objectives
- Set stage deadlines and complete ASAP
- Make the protocols simple and flexible
- Require teamwork, trust, and consensus building
- Time-consuming, particularly for WG leaders
- Often more complicated than expected
- Need effective coordinating center/coordinator



# Acknowledgements

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- National Cancer Institute