

# Framingham Heart Study: A Review of Research Design



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## Contents

### Original Cohort

- Objectives
- Sampling
- Examination
- Maintenance of validity
- Advanced Screening Tools

### Comparison of

Original Cohort, Offspring Cohort & New offspring spouse Cohort, Third Generation Cohort, Omni Cohort 1 & Omni Cohort 2

### Supporters

- U.S. Public Health Service
- National Heart Institute, NIH
- Contract with Boston University and NHLBI

## Original Cohort 1948

### Cohort study

A group of individuals with a common characteristic or sharing same experiences who are followed over a period of time [1].

e.g. Framingham Heart Study is a prospective investigation of the epidemiology of CHD.

It is a population based open cohort (Figure 1).



**Figure 1**

### Purpose

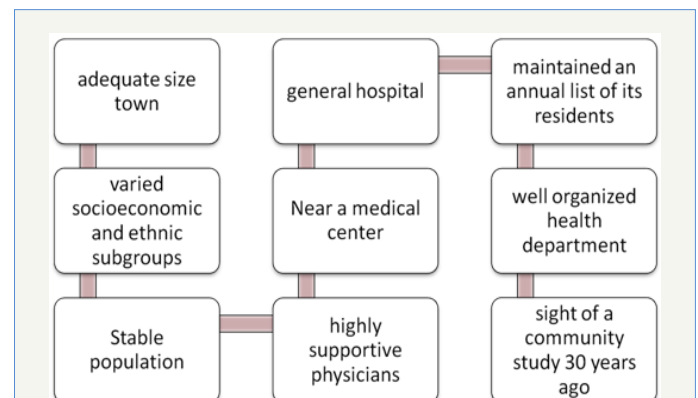
To study the epidemiology of CHD

### Objectives

- To study the incidence and prevalence and risk factors of cardiovascular disease (CVD)

ii. To study familial patterns, trends in CVD incidence and its risk factors over time

iii. To estimate the incidence rates of disease and to describe the natural history of cardiovascular disease (Figure 2).



**Figure 2:** Characteristics that made Framingham suitable for a long-term epidemiological study. Feinlieb (1983).

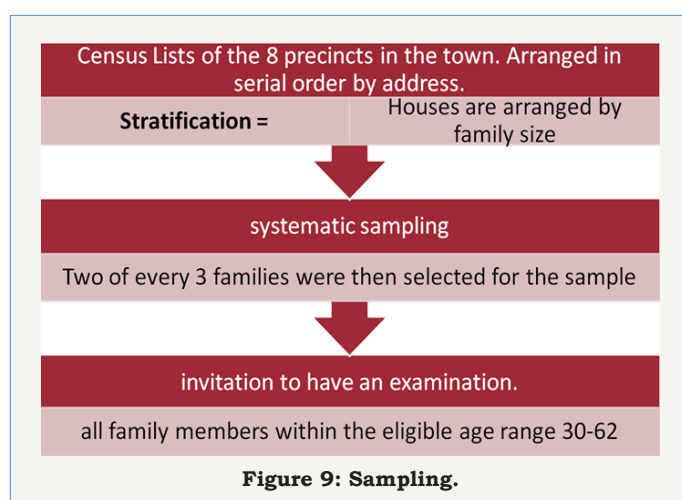
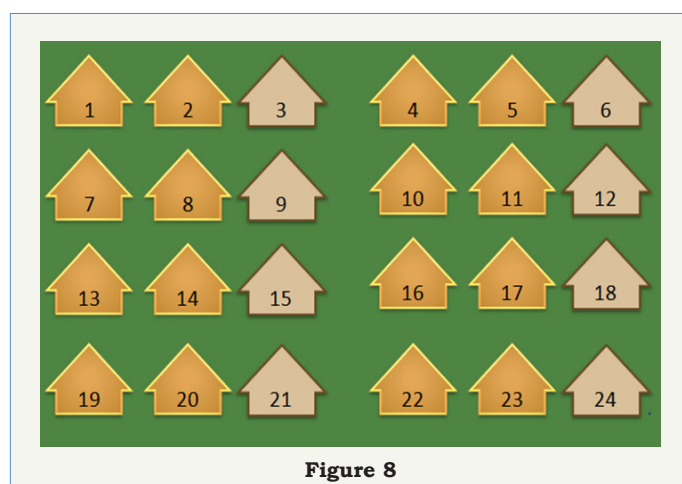
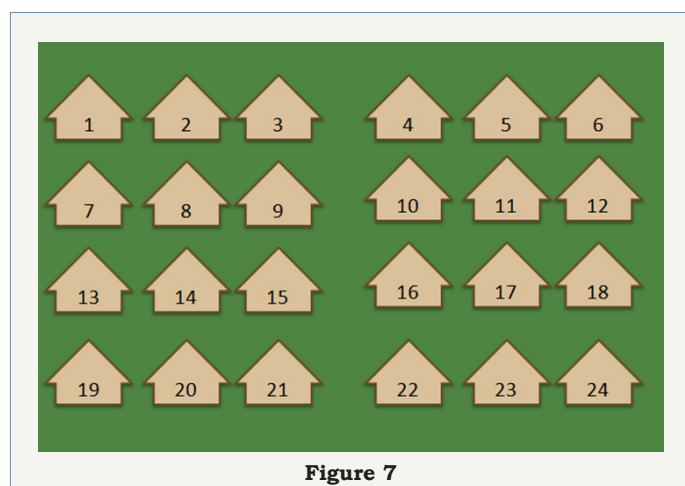
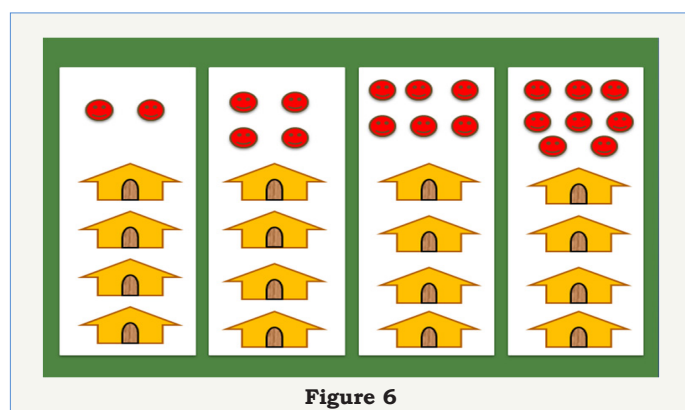
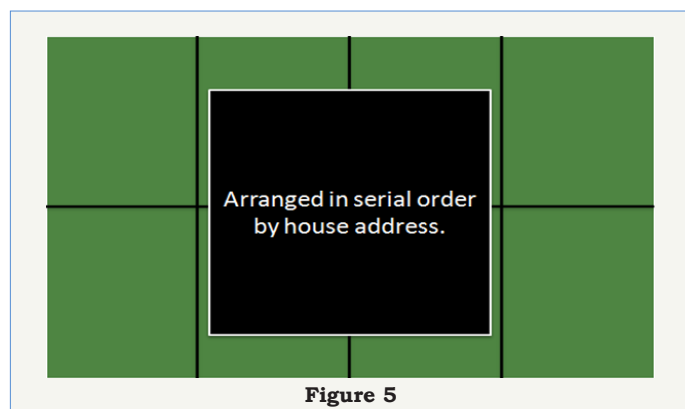
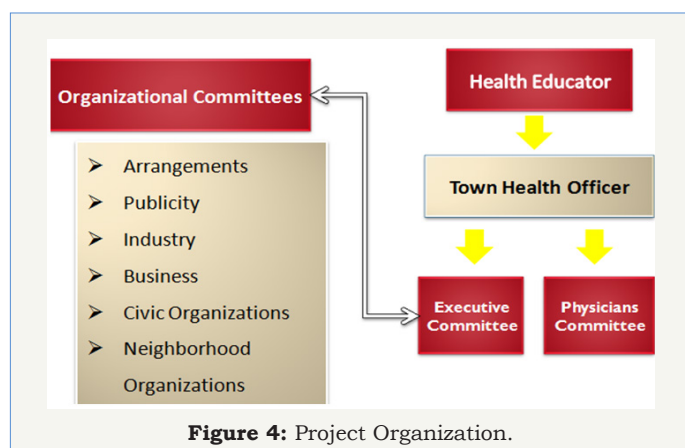
The Framingham investigators have always been aware that the site may not be representative of the United States and have made repeatedly comparisons with other regions to test its generalizability (Figure 3-9).



**Figure 3**

## Sample Size

Total population of town (30-62 years) =10,000.



Desired sample size = 6,000

Because only 6,000 exams could be given in this two year cycle

So a 2/3<sup>rd</sup> sampling ratio was applied to yield the 6,000.

They estimated that 5,000 would be free of CVD at the baseline exam, a large enough sample to produce statistically stable data (Table1 & 2).

**Table 1:** Response of the Selected Sample.

Sampling	Sample Size
Formal sampling	6,587
Duplicate names	-80
Potential sample	6,507
Turn out Sample	4469

**Table 2:** Response Rate 68.7%.

	Sample	Free of CVD
Respondents	4469	4393
Addition of volunteers	888	
Returned for a second visit	740	734
Total	5,209	5127

## Consent

The documentation of informed consent began in 1971 1st exam cycle of the Offspring Cohort and then the 12th exam cycle of the Original Cohort [2-5]. The research protocols of the Framingham Heart Study are reviewed annually by the Institutional Review Board of the Boston University Medical Center and by the Observational Studies Monitoring Board of the National Heart, Lung and Blood Institute.

I agree to

- i. Participate in the FHS clinic examination and studies
- ii. Provide a blood sample from which genetic material (DNA and other components) to be used in the genetic studies
- iii. To allow researchers from commercial companies to have access to my DNA and genetic data this may be used to develop new lab tests or treatments.

## Research Design

### Pre-Testing (September 29, 1948)

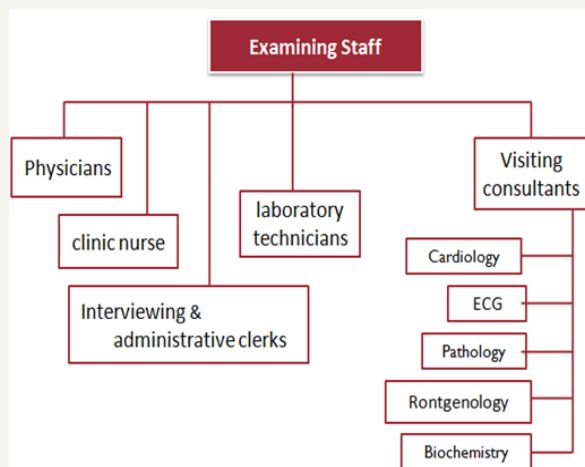
The FHS examined its own staff members.

Exam (October 11, 1948)

Follow up

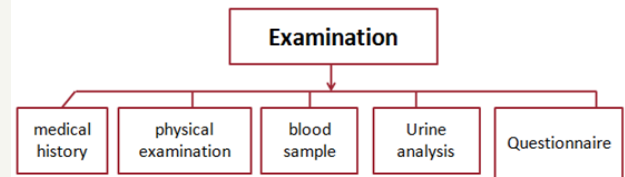


**Figure 10:** Research design.

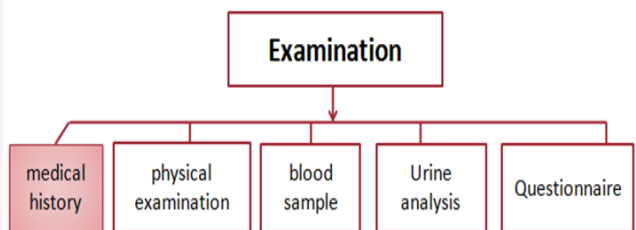


**Figure 11:** Research design.

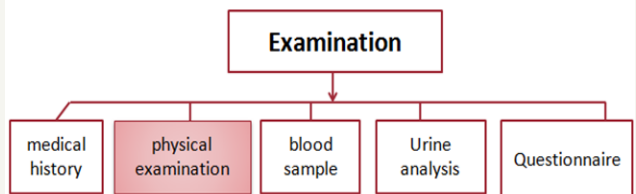
Biennial examinations of subjects (for morbidity and mortality development) (Figure 10-17).



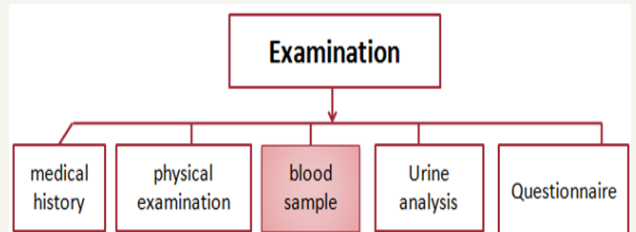
**Figure 12**



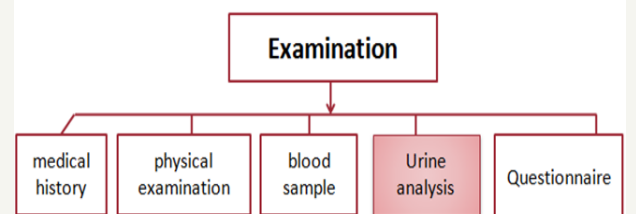
**Figure 13**



**Figure 14**



**Figure 15**

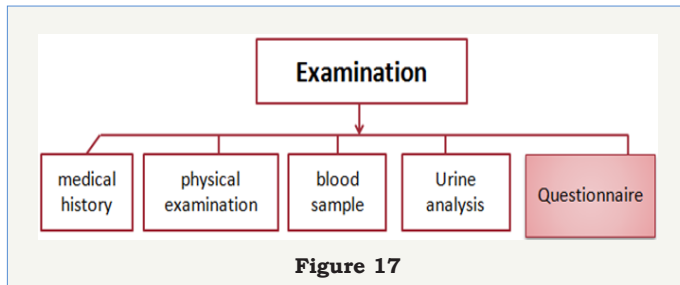


**Figure 16**

## Validity Maintenance

- i. A Clinic Protocol Manual

- ii. Periodic “site visits”
- iii. A separate Pulmonary Function Manual
- iv. Biochemical analysis
- v. All diagnoses were verified
- vi. Review of each death



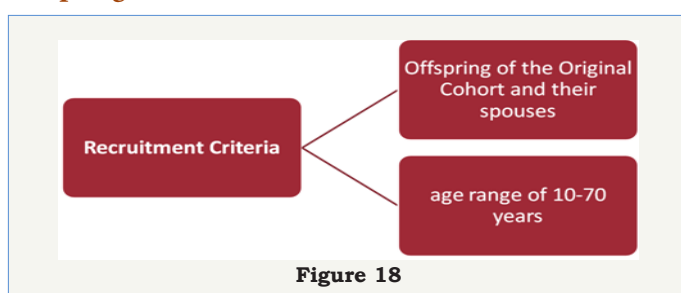
### Failure to appear for re-examination

- i. Kept track of the clinical status by community surveillance [6].
- ii. Persons who moved out were likely to be healthier
- iii. Persons who stopped coming while still resident were seriously, even terminally, ill (Table 3).

**Table 3:** Advanced Screening Tools.

Tests	Old tools	Advanced Tools
Blood Sugar Test	Exam 18	Exam 19-23
	Random blood sugar	HBA1C
Bone Density Test	Exam 8	Exam 22-24
	X-Ray	DEXA Scan
Electrocardiogram	Exam 18	Exam 23, 24
	ECG 2 hr ambulatory	Exercise Tolerance Test

### Offspring Cohort



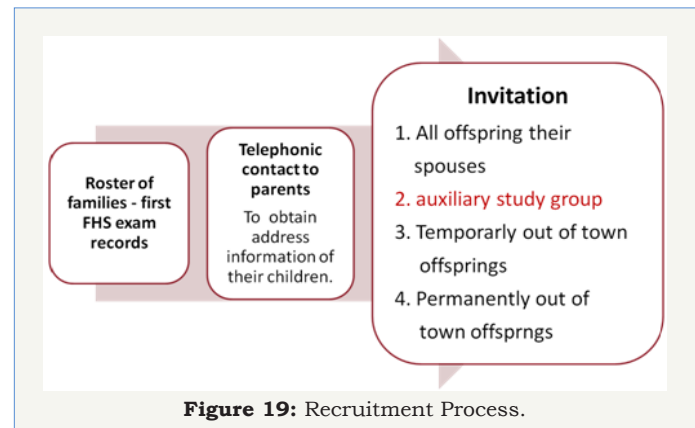
A prospective epidemiologic study of CHD in young adults to study familial clustering of the disease and its risk factors [7].

1971-1975: Follow up after 4 years (Figure 18 & 19).

### Third Generation Cohort

To gather phenotypic and genotypic information

2002-2005: Follow up after every 6 years. Participants in the Offspring Cohort at their 6th and 7th examination cycles provided updated lists:

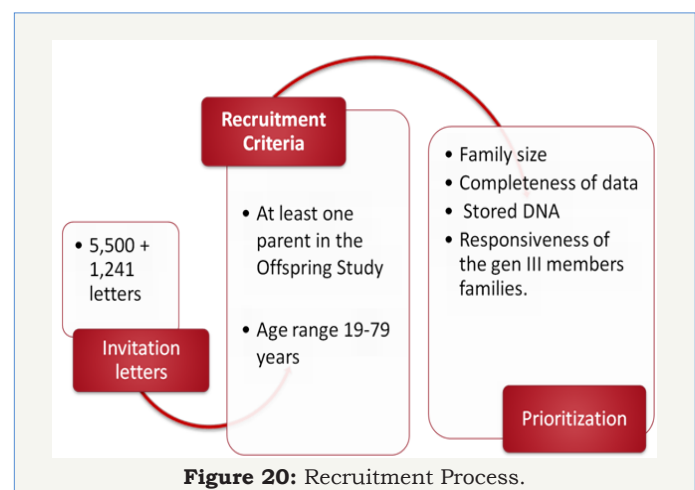


Family description form

- i. Names
- ii. Relationships
- iii. Residential addresses
- iv. Telephone numbers
- v. Gender
- vi. Birth dates of their children
- vii. Identification
- viii. Dissemination of study objectives to the community.
- ix. Invitation
- x. Examination of consenting participants

### Primary focus

To study large multi generational extended family groups. 3,975 /4,095 participants were members of 879 larger FHS extended families (Figure 20).



### New Offspring Spouse Cohort

Addition of the data and cell lines of Offspring Spouse Cohort to improve the statistical power for studying families at FHS, 2003-2005 [8].

## Recruitment Criteria

- Spouses of Offspring cohort participants who were not initially enrolled
- With at least two children in the Third Generation cohort.

## Omni Cohort

Reflecting increasing diversity of the community

Omni Cohort 1 1994

Omni Cohort 2 2005

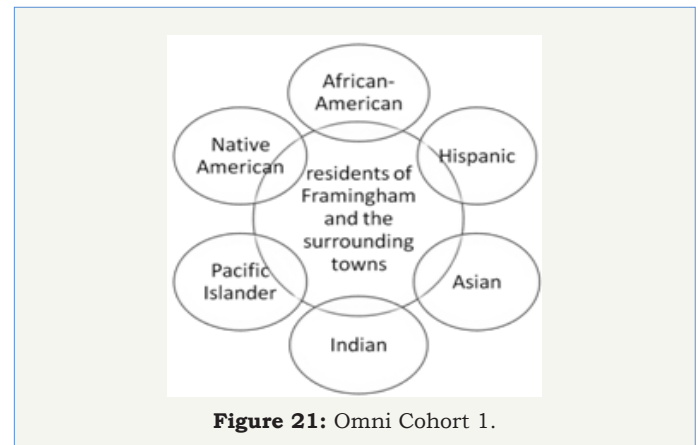
## Omni Cohort

- Officially known as minority over sampling
- Ethnic minority residents of Framingham
- A minority group in this study is considered one that is racially distinct from the original cohort, which was defined as white.

## Omni Cohort 1

Need to establish a new group of participants reflecting the

increasing diversity of the community (Figure 21)



## Omni Cohort 2 (2005)

**Purpose:** To allow an ethnically diverse comparable cohort to the Generation III cohort.

**Recruitment criteria:** No relationship to someone in the first generation had to be claimed to be able to participate (Table 4-8).

**Table 4:** Purpose

Original Cohort	To study the expression of CHD in a normal population and to determine the factors predisposing to the development of the disease.
Offspring Cohort	To study the epidemiology of CHD in young adults.
3 <sup>rd</sup> Generation Cohort	To gather phenotypic and genotypic information
New offspring Spouse Cohort	To improve the statistical power for studying families at FHS
Omni Cohort 1	To reflect the increasing diversity of the community
Omni Cohort 2	To reflect the increasing diversity of the community with more sample.

**Table 5**

FHS cohorts	Recruitment Criteria	Age Range
Original Cohort	Normal population of Framingham and neighboring areas	30-62
Offspring Cohort	Offspring of the Original Cohort and the spouses of those offsprings	Oct-70
3 <sup>rd</sup> Generation Cohort	At least one parent in the Offspring Study	19-79
New offspring Spouse Cohort	Spouse of an Offspring who was never enrolled in the Framingham Heart Study	40 – 89
	At least two of his/her biological children participated in Exam 1 of Gen III.	
Omni Cohort 1	Ethnic minority residents of Framingham	20 – 70
Omni Cohort 2	It included many individuals related to / unrelated to the participants of Omni Cohort 1.	20 - 70+

**Table 6**

FHS Cohorts	Sample size	Folow up (years)	Latest Exam	Sample size left
Original Cohort	5209	2	32	40
Offspring Cohort	5124	4	9	2430
3 <sup>rd</sup> Generation Cohort	4095	6	2	3411
New offspring Spouse Cohort	103	5	2	68
Omni Cohort 1	506	5	4	301
Omni Cohort 2	410	6	2	321

Table 7

Exam Dates and Age Ranges as of 04/24/2014				
Original Cohort				
Exam	Exam Date Range	Age Range	Mean Age	Attendees
Exam 1	1945 - 1953	28 - 74	44	5209
Exam 2	1950 - 1955	31 - 65	46	4792
Exam 3	1952 - 1956	32 - 67	48	4416
Exam 4	1954 - 1958	34 - 69	50	4541
Exam 5	1956 - 1960	37 - 70	52	4421
Exam 6	1958 - 1963	38 - 72	54	4259
Exam 7	1960 - 1964	40 - 74	55	4191
Exam 8	1962 - 1966	42 - 76	57	4030
Exam 9	1964 - 1968	44 - 78	59	3833
Exam 10	1966 - 1970	46 - 80	61	3595
Exam 11	1968 - 1971	49 - 81	62	2955
Exam 12	1971 - 1974	50 - 83	64	3261
Exam 13	1972 - 1976	53 - 85	66	3133
Exam 14	1975 - 1975	55 - 88	68	2871
Exam 15	1977 - 1979	57 - 89	69	2632
Exam 16	1979 - 1982	59 - 91	70	2351
Exam 17	1981 - 1984	61 - 93	72	2179
Exam 18	1983 - 1955	63 - 94	74	1825
Exam 19	1985 - 1958	65 - 96	75	1541
Exam 20	1986 - 3_390	67 - 97	77	1401
Exam 21	1988 - 1992	69 - 99	79	1319
Exam 22	1990 - 1994	72 - 101	80	1166
Exam 23	1992 - 1996	73 - 101	81	1026
Exam 24	1995 - 1995	76 - 103	83	831
Exam 25	1997 - 1999	78 - 104	84	703
Exam 26	1999 - 2001	79 - 103	86	558
Exam 27	2002 - 2003	82 - 104	87	414
Exam 28	2004 - 2005	84 - 104	89	303
Exam 29	2006 - 2007	85 - 102	91	218
Exam 30	2008 - 2010	88 - 102	92	141
Exam 31	2010 - 2011	90 - 99	92	91
Exam 32	2012 - 2014	93 - 106	96	40
Offspring Cohort				
Exam	Exam gate Range	Age Range	Mean Age	Attendees
Exam 1	1871 - 1975	5 - 70	36	5124
Exam 2	1979 - 1983	17 - 77	44	3863
Exam 3	1983 - 1987	28 - 77	48	3873
Exam 4	1987 - 1991	22 - 81	52	4019
Exam 5	1991 - 1995	26 - 84	55	3799
Exam 6	1995 - 1998	29 - 86	59	3532
Exam 7	1998 - 2002	33 - 90	62	3539
Exam 8	2005 - 2008	40 - 93	67	3021
Exam 9	2021 - 2014	46 - 913	71	2430
Generation 3 Cohort				



Exam	Exam Date Range	Age Range	Mean Age	Attendees
Exam 1	2002 - 2005	19 - 72	40	4095
Exam 2	2005 - 2011	24 - 78	47	3411
<b>New Offspring Spouse Cohort</b>				
Exam	Exam Date Range	Age Range	Mean Age	Attendees
Exam 1	2003 - 2005	47 - 85	65	103
Exam 2	2006 - 2011	53 - 90	70	68
<b>Omni 1 Cohort</b>				
Exam	Exam Date Range	Age Range	Mean Age	Attendees
Exam 1	1994 - 1998	27 - 78	52	506
Exam 2	1999 - 2001	33 - 83	55	405
Exam 3	2007 - 2008	39 - 89	62	298
Exam 4	2011 - 2014	44 - 88	66	301
<b>Omni 2 Cohort</b>				
Exam	Exam Date Range	Age Range	Mean Age	Attendees
Exam 1	2003 - 24305	20 - 80	43	410
Exam 2	2009 - 2011	25 - 85	48	321

**Table 8**

FHS Cohorts	Men	Women	Total
Original Cohort	2336	2873	5209
Offspring Cohort	2483	2641	5124
3 <sup>rd</sup> Generation Cohort	1913	2182	4095
New offspring Spouse Cohort	47	56	103
Omni Cohort 1	212	294	506
Omni Cohort 2	177	233	410

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