FAMILY RESEARCH MATTERS



# NON-STICK KITCHENWARE



A scientific discovery is a fine thing in itself, but it does not help the world until it is put on a business basis

HENRY FORD

# HEALTH SERVICES RESEARCH

#### EFFECTIVENESS

OUTCOMES

EFFICIENCY

RESOURCES

EQUITY

DENOMINATORS

#### THE "GENETICISATION" OF SOCIETY

At its extreme, this reliance may allow governments to evade their responsibility for developing environmental, social and economic policies that acknowledge the association of poverty, poor housing and unemployment with physical and psychological illness

Kumar S Lancet 1999;354:1992-3



# THE END

OF

#### UNCERTAINTY ?



\* \* \* \* \* THE NEWS OF THE WORLD

#### PHARMACOGENETICS ?

"The era of personalised medicine, which would see drugs tailored to an individual's genetic make-up, is at least 15-20 years away, according to a report by the Royal Society.

Using genetic tests, drug companies are increasingly able to identify which drugs will work best for different patients.

But Sir David Weatherall, who chaired the Royal Society's working group, said not enough was known about the genetic causes of disease yet for so-called pharmacogenetics."

Weekly Guardian 30 September 2005

#### CURRENT USES OF GENETIC TESTING

Confirming diagnosis when symptoms arise

Investigating a family history of late onset disease e.g. Huntington's Disease

Checking for carrier status in recessive disorders e.g. cystic fibrosis

Prenatal screening e.g. Down's syndrome

Investigation of familial cancers e.g. breast, colorectal, ovary

#### **FUTURE USES**

Cancer Diabetes Coronary heart disease Asthma Osteoporosis Schizophrenia Dementia

#### BALANCE OF CARE

Referral centres

General practitioners with special interests

Genetics nurse counsellors

Primary health care professionals

Self care



#### WHAT SHOULD PRIMARY CARE NOT DO ?

# PRIMUM NON NOCERE

I feel like someone has died.

Part of ME has died - the hopeful part

Bloch et al Am J Human Genetics 1990;46:1-4 Someone to love

Something to do

Something to hope for

**Robert Louis Stevenson** 



#### WHAT SHOULD PRIMARY CARE DO?

#### High risk strategies

# Celebrating 30 years of the MIDSPAN Studies





# SCOTLAND

# GLASGOW

# RENFREW

PAISLEY

#### PAISLEY, RENFREW AND GLASGOW



#### Celebrating 30 years of the MIDSPAN Studies



# PAISLEY TOWN HALL, 26TH





### **BLOWING HARI**

#### **INTO A TUBE**



# 15 YEAR FOLLOW UP BY BLOOD PRESSURE QUINTILE

Q2 Q3 Q4 Q5 Q1 Total Hig Low h Number of men 800 802 799 801 4002 800 102 133 136 599 75 Coronary seaths deaths 17 17 22 30 57 143

**MIDSPAN Renfrew and** 

**Daielov Study** 

# False positives

False negatives

#### real people talking about heart disease

# 

#### **HEARD IT ALL BEFORE?**

Heart Health MAKING SENSE OF THE MESSAGES AND MOVING FORWARD >>

Heard it all before? • Will it happen to me? What about money? • What if heart disease runs in the family? Food, what can I believe? • A good way to go? • Useful contacts! Lay constructions of a family history of heart disease: Potential for misunderstandings In the clinical encounter

Kate Hunt Carol Emslie Graham Watt

Lancet 2001;357:1168-71

# PERCEPTIONS OF FAMILY WEAKNESS DUE TO CHD

- Only 1 in 4 sons and 1 in 3 daughters with a parental CHD death consider that they have a "family weakness" due to CHD
- Working class sons are least likely to attribute a parental CHD death to a "family weakness"

JECH 2000; 54: 859-63

# SHONA - MIDDLE CLASS

"For everyone fit ...you think there's another bloke going about smoking and beer belly out to here and living for ever and ever and seeming to have no adverse effects anyone can see, what's going on?"

# UNCLE NORMAN

#### BMJ 2001;323:1487-91



# PHIL - WORKING CLASS

"I know a few people that have had heart problems and they'd be the last people you'd think of, you read in the paper about people that's out jogging and athletes that have heart problems, guy, one of the fittest men you would look at on the television is Graeme Souness, he's had a triple by-pass operation, he'd be the last person on earth you'd think." THE LAST PERSON ......

If the British working man backs a horse or dog because of its breeding, why should not the better bred members of the House of Lords be worthy of our trust in their inherited powers of leadership?

Editorial, Daily Telegraph, 1970s

#### FAMILY HISTORY AS A CLINICAL TOOL

The place of family history information in clinical encounters?

What information?

Collected by whom?

How stored and retrieved?

Confidentiality within families?

Other information about the family?

# When did you last see your father?



#### **GENE DISCOVERY STUDIES**

#### WHAT TO LOOK WITH ?

#### WHAT TO LOOK FOR ?

WHERE TO LOOK ?




### LOOKING FOR STRONG SIGNALS

## IN FAMILY PRACTICE





# Consanguinity

#### A RHEUMATIC FAMILY

W. N. PICKLES, M D LOND, M R C P

AFTER many years in country practice, my experience of rheumatic fever and rheumatic heart disease had been so meagre that I felt justified in considering them locally very rare. It then dawned on me that waitfrees discovered before the relationship. It was found possible to work out a family tree and to show that out of 53 descendants of a man — himself a victim — who died long before my time. 23 had suffered with rheumatic fever or had unmistakeable signs of mitral stenosis. Besides the original victim I who died long before my time. 23 had suffered with rheumatic fever or had unmistakeable signs of mitral stenosis. Besides the original victim I had to accept hearsay evidence of but three others, having myself attended and examined the remaining 20. Of these, 10 have died; one from an accident in youth, the others from heart disease between the ages of 48 and 70. Four with rheumatic fever have come under my care — 2 only developing heart lesions. Nine with such lesions gave a history of rheumatic fever and 5 lesions were discovered without relevant history. One young woman developed mitral stenosis after tonsillitis and her sister after tonsillectomy.

The causation of rheumatic fever is rightly one of the most important objects of research at the present time, and as environmental influence is bound to loom large, it is as well to remember the existence of such families.

It is interesting and important to know what manner of people are being



#### Black circles indicate members of the family with a history of rheumatic fever or signs of mitral stenosis

studied and something about their lives. After 30 years' close experience, I have no hesitation in singling these people out as among the most outstanding in the district. With insignificant exceptions they are prosperous, well-housed and well-fed. In personal experience they are much above the average, tail and broad with an unselfconscious dignified carriage. They have a proper and justified family pride and a sense of inheritance, claiming descent from a follower of Alan of Britany upon whom the Conqueror bestowed Richmondshire. They are as a rule successful farmers but a switch-over to other occupations has simply meant adaptation of talents and success in a new sphere.

The victims of mitral stenosis do not seem to follow the usual rules for this disease. The men live the strenuous lives of hil farmers. The women, besides doing the heavy work of the farmer's wife, bear children and feed them at the breast, and all positively refuse to believe that any care is needed. Yet none of these sufferers has up to the present died from heart disease at an early age. The diagram shows the sufferers in black and spouses are omitted. In no instance was the spouse rheumatic, so that the story is uncomplicated.

It is futile to speculate on the destiny of this remarkable family. "It is not observed in history that families improve with time" may well prove true in a medical sense. It may be that environment has hitherto been so favourable for this family that it has helped its members in part to elude the shackles of inheritance.

I am indebted to Miss Marie Hartley, of Askrigg, for the diagram

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uary 2000

173

"It may be that environment has hitherto been so favourable for this family that it has helped its members in part to elude the shackles of inheritance".

Lancet, 21<sup>st</sup> August

# **Interaction of Genes and Environment**



**Susceptibility to Cancer** 

# FAMILY EPIDEMIOLOGY

DISTRIBUTION OF OFFSPRING BLOOD PRESSURES ACCORDING TO TOP AND BOTTOM QUINTILES OF PARENTAL BLOOD PRESSURES



#### RELATING NUMBERS OF OFFSPRING ACCORDING TO TOP AND BOTTOM QUINTILES OF PARENTAL BLOOD PRESSURE DISTRIBUTIONS



# FAMILY STUDY - 1

# Ladywell Family Blood Pressure Study Ladywell Medical Centre, Edinburgh

603 families

864 offspring 16-24 years





# STUDY PROTOCOL

Hospital admission

Fasting overnight

Oral glucose tolerance test

Mental arithmetic













Figure 2. Dermal vasodilatation in response to heat and ischemia in subjects from the four corners. Increasing flux was measured after heating to 42°C (a) and, in addition, after 5 min ischemia (b). Bars are means. Analysis of variance for the four corners was significant to P < 0.0001 for both variables, and P values shown refer to subsequent comparison of corners with corner OH/PH by Fisher's probability of least squares difference test. \*\*P < 0.001; \*\*\*P < 0.0001.

## CHARACTERISTICS OF OFFSPRING WITH HIGH BP WHOSE PARENTS ALSO HAVE HIGH BP

- Increased pulse rate and adrenaline response to a glucose load (Circulation 1997;96:556-61)
- Increased glomerular filtration rate (Hypertension 2000;321:952-7)
- Reduced number of dermal capillaries resulting in increased minimal vascular resistance (JClinInvest 1997;99:1873-9)
- Increased in vivo responsiveness to glucocorticoids (Hypertension 1998; 31:891-5)





Figure 1. The four corners model of contrasting predisposition to high blood pressure. Blood pressures are plotted as Z-scores (i.e., SDs from the age-adjusted mean) for offspring and as Z-scores of the arithmetic mean for parents. The dashed lines show the cutoffs  $(\pm 0.35 \text{ SD})$  used to define corners containing at least 50 offspring. The number of offspring in each corner are shown. These figures include both males and females, but only males were used in the current study. Only a representative sample of the data points are shown for clarity.

### THE NEW GENETICS IN CLINICAL PRACTICE

- Genetics will provide a taxonomy of disease that is based on biochemical mechanisms rather than phenotype
- Genetic variation will be another form of "risk factor" and will permit early treatment and directed screening
- Genetic information is likely to transform the practice of clinical medicine

Professor John Bell BMJ 1998; 316:1618-20



# MIDSPAN FAMILY STUDY (Renfrew and Paisley)

- 15406 men and women aged 45-64 in 1972-76
- 79% of general population
- 4064 married couples
- 25 year follow up for mortality, cancer incidence and hospital admissions

No. 37088

TUESDAY, SEPTEMBER 7, 1993

# SEARCH FOR 3000 GUNEA PIG' KIDS Children of 70s families sought for new health tests

A MASSIVE search has been launched to find thousands of people who took part in a unique health study carried out in Paisley and Renfrew more than 20 years ago.

They are wanted to help in a new survey which will investigate why some families experience heart disease and cancer more than others.

The move comes as findings of the first survey, carried out between 1972 and 1976, show that for a given level of smoking the rate of lung cancer in Paisley

#### By Anne Dalrymple

and Renfrew is twice as high as in other populations.

24p

Results also show that the statistics are the same for heart attacks and cholesterol count.

This time round, however, it's the children of the 4000 parents involved in the original study who are desperately wanted by researchers at Glasgow University.

"Out of the 15,000 people who originally took part there are just over 4000 married couples," said Dr Graham Watt one of the research team. "The problem for us is trying to contact them. We need their help to establish the whereabouts of their children so that we can go on and ask them if they would be willing to take part in this new study some 20 years on.

"On the basis of our own pilot study it is estimated that there are about 2000 to 3000 children still living in the Paisley, Renfrew and Glasgow areas."

"Our task is to try and find them." Dr Watt added: "Despite all the advances in molecular biology, a huge limiting factor in understanding major diseases is the problem of finding populations which are suitable to study. "There is probably nowhere else in the world just now where it is possible to carry out a study of the type that we propose.

Daily Express

"It would take other researchers 20 years to establish a similar opportunity to the one which exists at present in Paisley and Renfrew."

Between 1972 and 1976 when the original study was carried out 80 per cent of the population in Paisley and Renfrew took part. Measurements of blood pressure, cholesterol, glucose, height, weight and lung function were all taken.

It is the only study of cardiorespiratory disease and risks whose results can be

applied directly to health problems of people in the West of Scotland.

<sup>6</sup> Dr Watt said: "The results have been very useful in explaining why there is so much heart disease and cancer in this part of the world. What we want to look at now is why some families suffer from these diseases more than others."

"The only people who can help us today with the vital information we need are the children of the couples involved in the original study."

If you know where they are now you can contact the research team on 041-9 46-7120 extension 1446 for more information.

# FAMILY STUDY - 2

MIDSPAN Family Study Paisley and Renfrew

1477 Families

1040 Sons 30-59 yr 1298 Daughters 30-59 yr

## **FAMILY CHANGES IN SOCIAL CLASS**

**NON-MANUAL** 

#### MANUAL

OCCUPATIONS OCCUPATIONS

- FATHERS
   33%
   67%

   SONS
   55%
   45%

   MOTHERS
   47%
   53%
- DAUGHTERS 77% 23%

## **FAMILY CHANGES IN SMOKING**

CURRENT	NEVER	FORMER	
	SMOKERS	SMOKERS	SMOKERS
FATHERS	20%	35%	55%
SONS	38%	35%	26%

 MOTHERS
 40%
 8%
 52%

 DAUGHTERS
 46%
 29%
 24%

## FAMILY CHANGES IN RESPIRATORY SYMPTOMS

SPUTUM HAY FEVER ASTHMA

FATHERS	24%	5%	1.4%	
SONS	14%	15%	4.9%	
MOTHERS	13%	6%	2.8%	
DAUGHTERS	7%	20	% 8	.0%

## **FAMILY CHANGES IN HEIGHT**

FATHERS	170.5 cm	(5 feet 7 inches)
SONS	174.4 cm	(5 feet 9 inches)
MOTHERS	158.4 cm	( 5 feet 2 inches
DAUGHTERS inches )	161.	1 cm (5 feet 3



### MATERNAL AND PERSONAL CIGARETTE SMOKING SYNERGISE TO INCREASE AIRFLOW LIMITATION IN ADULT OFFSPRING

In adult offspring who smoke, the risk of prevalent COPD increases by 70% per 10 cigarettes per day of maternal smoking

The effect of 10 cigarettes per day of maternal smoking is numerically equivalent to 10 years personal smoking.



Am J Respir Crit Care Med 2004, 169, 479-87

FEV1



#### CHOLESTEROL



#### HEIGHT


#### **BODY MASS INDEX**



### TRENDS IN BMI AND OBESITY

	Prevalence of obesity (BMI>30)	Mean (BMI kg/m²)
Fathers 1972-76	9.1%	26.0
Sons 1996	18.4%	26.7
Mothers 1972-76	15.4%	25.8
Daughters 1996	17.5%	26.2

### INTER-GENERATIONAL TRENDS IN DISTRIBUTION OF BODY MASS INDEX

Fathers and Sons BMI Distributions



#### INTER-GENERATIONAL TRENDS IN DISTRIBUTION OF BODY MASS INDEX



# Prevalence of BMI>30kg/m2 in sons and daughters reporting high and low level of physical activity, by mid-parental BMI





Midparental BMI groups

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FAT FAMILIES ARE GETTING FATTER

Niveen Abu-rmeileh, Alex McConnachie, Mark Upton Mike Lean, Graham Watt

Submitted for publication



### PROGRESS

REQUIRES

BALANCED

ACTIVITY

## FAMILY RESEARCH MATTERS