HORMONES AND SEXUAL FACTORS IN HUMAN CANCER AETIOLOGY

editors:
j. p. wolff, j. s. scott

HORMONES AND SEXUAL FACTORS IN HUMAN CANCER AETIOLOGY

Proceedings of the 2nd Annual Symposium
of the European Organization for Cooperation
in Cancer Prevention Studies (ECP)
Brugge, Belgium, June 22–23, 1984

Editors:

J.-P. Wolff
Institut Gustave Roussy, Villejuif, France

J.S. Scott
Department of Obstetrics and Gynaecology,
University of Leeds, Leeds, UK

1984

Excerpta Medica, Amsterdam - New York - Oxford

International Congress Series No. 650
ISBN 0 444 80645 8

Published by:

Elsevier Science Publishers B.V.
P.O. Box 211
1000 AE Amsterdam
The Netherlands

Sole distributors for the USA and Canada:

Elsevier Science Publishing Company Inc.
52 Vanderbilt Avenue
New York, NY 10017
USA

Library of Congress Cataloging in Publication Data

European Organization for Cooperation in Cancer Prevention Studies.
Symposium (2nd : 1984 : Bruges, Belgium)
Hormones and sexual factors in human cancer aetiology.

(International congress series ; no. 650)
Contains the proceedings of the 1984 Symposium on 'Hormone and Sexual Factors in Human Cancer Aetiology'.
Includes bibliographies and index.
1. Carcinogenesis--Congresses. 2. Generative organs, Female--Cancer--Etiology--Congresses. 3. Cancer--Endocrine aspects--Congresses. 4. Cancer--Sex factors--Congresses. 5. Oral contraceptives--Side effects--Congresses. I. Wolff, J.-P. II. Scott, J.S. III. Title. IV. Series. [DNLM: 1. Hormones--adverse effects--congresses. 2. Neoplasms--etiology--congresses. 3. Sex Behavior--congresses. W3 EX89 no. 650 / QZ 202 E897 1984h]
RC268.5.E96 1984 616.99'4071 84-25845
ISBN 0-444-80645-8 (U.S.)

Printed in The Netherlands

FOREWORD

ECP (European Organization for Cooperation in Cancer Prevention Studies) was established in 1981 with the object of fostering the development of joint studies on a European basis in this field as the activity of EORTC (European Organization for Research on Treatment of Cancer) was restricted to research on cancer treatment.

The method chosen to achieve the aim was to establish working parties to deal with particular cancers or aspects of cancer aetiology, exploring the opportunities for advance on a cooperative European basis. It was also decided to hold an annual symposium to draw general attention to a field in which there seemed to be particular opportunities for progress in matters of prevention.

This volume contains the proceedings of the 1984 Symposium on 'Hormones and Sexual Factors in Human Cancer Aetiology'. The general plan of the Symposium was formulated by the group established to deal with 'Sexual Factors and Cancer' with which we were associated. We were fortunate to obtain contributions of an outstandingly high calibre from a wide range of European workers, all extremely distinguished in their field. The papers and the discussion which followed them indicated that, in relation to the group of cancers considered, exciting opportunities for prevention are developing particularly with regard to endocrine and viral factors. They also suggest that as so much expertise in the field lies with European workers, there must be high hopes that joint studies involving European countries will lead to important practical advances. This is the approach which ECP aims to foster.

We are indebted to the speakers represented in this publication for their prompt provision of manuscripts. We are also grateful to the WHO, UICC and the EEC Commissioner for Social Affairs for their sponsorship, and to the City of Bruges for allowing us to hold the sessions in the prestigious Belfry building. The financial support of Farmitalia Carlo Erba is again acknowledged with gratitude.

Due to our tight schedule for publication several of our contributors were unable to let us have manuscripts in the time available. Dr. Guy Blaudin de Thé of Lyon spoke on 'Viruses, sexually related cancers and prevention' and Prof. H. zur Hausen of Heidelberg on 'The role of papillomaviruses in gynaecological cancer'. These eminent experts in the virology field gave authoritative presentations on the background of knowledge relevant to the virological aspects. Prof. F. Di Re of Milan gave an outstanding presentation on 'Contribution of conization'.

The 1985 Symposium will be on 'Diet and Human Carcinogenesis' and will be held in Aarhus, Denmark, from 19th–21st June.

J.S. Scott
Dept. of Obstetrics and Gynaecology,
University of Leeds, Clarendon Wing,
Belmont Grove, Leeds LS2 9NS,
England.

J.-P. Wolff
Institut Gustave-Roussy,
39 à 53 Rue Camille Desmoulins,
94800 Villejuif Cedex,
France.

Contents

IV World Health Organization Academic Lecture

V Acquired Immune Deficiency Syndrome (AIDS)

VI Contraception and Cancer Risk

I. Introductory Lecture

Hormones and sexual factors in human cancer aetiology
J.-P. Wolff, J.S. Scott, editors

EPIDEMIOLOGY AND MORTALITY TRENDS OF SEX-RELATED CANCERS

JOZEF V. JOOSSENS and JEF GEBOERS

Division of Epidemiology, Sint-Rafaël University Hospital, Capucijnenvoer 33, B-3000 Leuven, Belgium.

INTRODUCTION

There are hardly any recent papers on mortality trends of cervix and corpus uteri cancers. With the Leuven Mortality Monitoring System (1), updated with the most recent data from WHO and from national sources (England and Wales, Finland, and Belgium), it is possible to give an overview of mortality trends, levels and interrelations not only for cervix and corpus uteri but also for breast and prostate cancer.

METHODS

Mortality data were available for 29 countries from 1961 to the latest available year, which ranges from 1978 to 1982, except for Czechoslovakia (1975). Among those are 22 western countries, six East European and Japan. Some small European countries, i.e. Luxembourg, Malta and Iceland, have been excluded from the analysis due to substantial random fluctuations in the mortality data. No data were available for the German Democratic Republic. Three truncated age adjusted mortalities were considered 25-44, 45-64 and 65 years and more (65+), except for prostate cancer where only the two oldest age groups were retained. The adjustment was done by the direct method using the European population as standard. The weighing factors were 14, 15, 14, 11, 7 and 4 for respectively the age groups 25-34, 35-44, 45-54, 55-64, 65-74 and 75+ years.

Trends were calculated using two mathematically independent statistics obtained from linear regression analysis, i.e. the slope of the regression equation (b) and the mean of the dependent variable (Y), in casu the chosen cancer mortality, over the appropriate time period. The annual change in mortality d (in %) was estimated by the formula $d=100*b/Y$. Significance was restricted to $p<0.05$. Mortalities are always given per million inhabitants of the same age group.

RESULTS

Table I shows the number of countries with significant mortality trends since 1961 in three age groups, separately for western countries and Japan, and for East European countries.

The subdivision cervix-corpus is probably less reliable in the oldest age group, and in some East European countries in the two younger age groups. This is suggested by the large number of increasing rates in cervical cancer (12/29)

in the 65+ group, whereas there is not a single country with increasing total uterus cancer. Increasing mortality rates are common in all considered age groups for breast and prostate cancer. This is even more frequent in East European countries, at least for breast cancer. Decreasing rates for breast cancer are observed in two countries only in the 25-44 group and in one in the 45-64 group. No country with significantly decreasing prostate cancer was found.

TABLE I

NUMBER OF COUNTRIES WITH SIGNIFICANT CHANGES IN CANCER MORTALITY FROM 1961 TO THE LATEST AVAILABLE YEAR

	Western Countries & Japan (n=23)						East European Countries (n=6)					
Age Group	25-44		45-64		65+		25-44		45-64		65+	
	-*	+*	-	+	-	+	-	+	-	+	-	+
Cervix	17	1	16	2	9	7	1	2	1	3	1	5
Corpus	18	0	22	0	13	1	4	0	4	0	4	0
Uterus	20	0	23	0	15	0	5	0	5	0	3	0
Fem. breast	2	8	1	17	0	18	0	5	0	6	0	6
Prostate			0	9	0	17			0	3	0	4

* - means a significant decrease in mortality; + is a significant increase.

The countries with best and worst results in terms of trends in cervix, corpus and total uterus cancer mortality are given in table II. The highest and lowest average cancer mortality levels are given for the same cancer localisations in table III.

Mortality trends for some Common Market countries are given in figures 1 to 6. Cervix cancer mortality (Fig. 1) in middle-aged females declined in most Common Market countries, the annual decreases ranging from 1.5 to 3.9 %. No significant changes were, however, observed for the Federal Republic of Germany and for Ireland, whereas a significant increase in cervix cancer mortality was found in Greece (5.4 %).

Corpus cancer mortality (Fig. 2), on the other hand declined in all Common Market countries, annual decreases ranging from 1.7 % in England and Wales to 4.8 % in the Federal Republic of Germany.

Combining both subcategories yielded total uterus cancer shown in figure 3. Again all countries showed significant decreases ranging from 1.3 % in Greece to 3.8 % in Belgium.

Female breast cancer is shown for two age groups, i.e. 45-64 and 65+ years, in

TABLE II

COUNTRIES WITH THE GREATEST ANNUAL INCREASE/DECREASE IN UTERINE CANCER SINCE 1961

Age Group	25-44		45-64		65+	
	Country	d*	Country	d	Country	d
Increase Cervix Cancer	Greece	+5.3	Greece	+5.4	Greece	+6.9
	Bulgaria	+1.7	Spain	+2.9	Spain	+4.0
	Hungary	+1.4	Poland	+2.1	Poland	+4.0
Decrease Cervix Cancer	Netherlands	-6.0	Canada	-4.5	Canada	-2.6
	Italy	-6.9	Finland	-4.7	Portugal	-3.5
	Finland	-9.3	USA	-4.9	USA	-4.2
Increase Corpus Cancer	---		---		Portugal	+2.0
	---		---		---	
	---		---		---	
Decrease Corpus Cancer	Germany FRG	-9.5	Romania	-5.5	Poland	-2.7
	Scotland	-9.9	Japan	-5.6	Hungary	-3.1
	Denmark	-10.4	Poland	-5.7	Romania	-4.3
Increase Uterus Cancer	---		---		---	
	---		---		---	
	---		---		---	
Decrease Uterus Cancer	Netherlands	-6.3	USA	-4.2	Japan	-1.9
	Japan	-6.8	Finland	-4.5	Belgium	-2.0
	Finland	-9.3	Japan	-5.0	USA	-2.9

* d = Annual change in mortality (in %) since 1961, calculated according to the formula listed in the text.

TABLE III

COUNTRIES WITH THE LOWEST AND HIGHEST AVERAGE UTERINE CANCER MORTALITY RATES

Age Group	25-44		45-64		65+	
	Country	$\bar{Y}$*	Country	$\bar{Y}$	Country	$\bar{Y}$
Highest Cervix Cancer	Denmark	96	Romania	284	Portugal	365
	Poland	63	Denmark	275	Denmark	289
	Romania	63	Poland	237	Romania	281
Lowest Cervix Cancer	Italy	9	Italy	46	Italy	57
	Greece	7	Greece	25	Spain	34
	Spain	4	Spain	25	Greece	33
Highest Corpus Cancer	Romania	53	Italy	294	Hungary	635
	Austria	53	Romania	285	Austria	622
	Hungary	50	Austria	280	Italy	553
Lowest Corpus Cancer	New Zealand	5	New Zealand	74	England & Wales	239
	Norway	5	Norway	73	Norway	226
	Australia	5	Australia	61	Australia	224
Highest Uterus Cancer	Romania	115	Romania	569	Hungary	899
	Denmark	107	Hungary	433	Austria	802
	Hungary	95	Portugal	416	Romania	708
Lowest Uterus Cancer	Australia	35	Bulgaria	201	Ireland	399
	Greece	32	Australia	197	Bulgaria	363
	Finland	30	Greece	167	Greece	305

* $\bar{Y}$ = Age-adjusted mortality rates (deaths/million/year), averaged over the time period 1961-last available year.

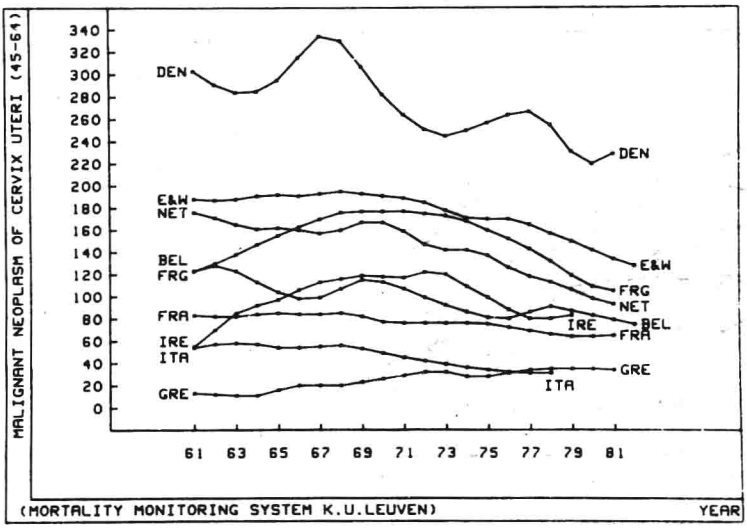

Fig. 1. Cervix uteri cancer mortality trends in nine Common Market countries (death rates per million, age adjusted 45-64 years).

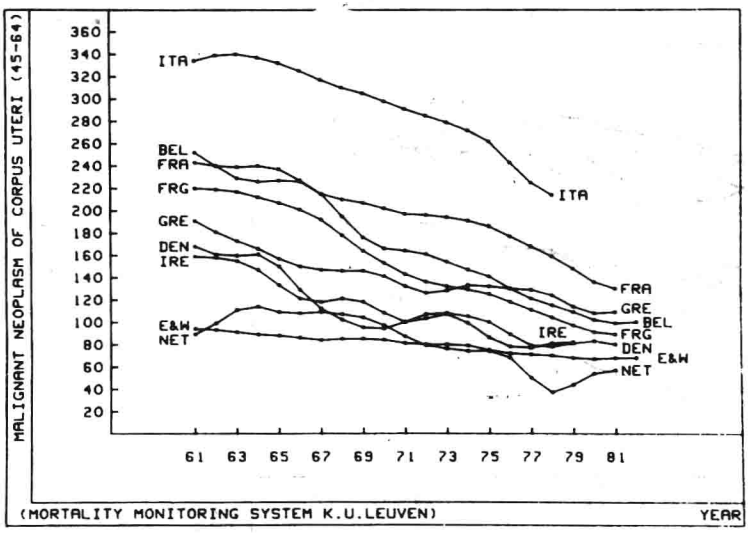

Fig. 2. Corpus uteri cancer mortality trends in nine Common Market countries (death rates per million, age adjusted 45-64 years).

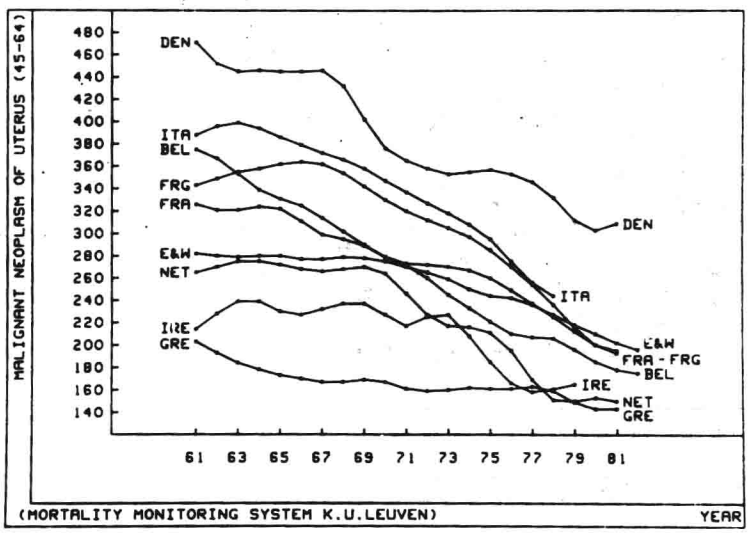

Fig. 3. Total uterus cancer mortality trends in nine Common Market countries (death rates per million, age adjusted 45-64 years).

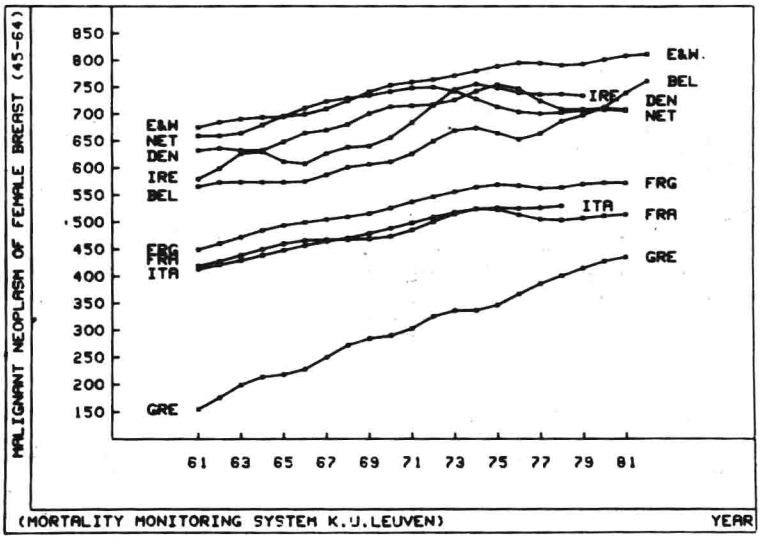

Fig. 4. Breast cancer mortality trends in nine Common Market countries (death rates per million, age adjusted 45-64 years).

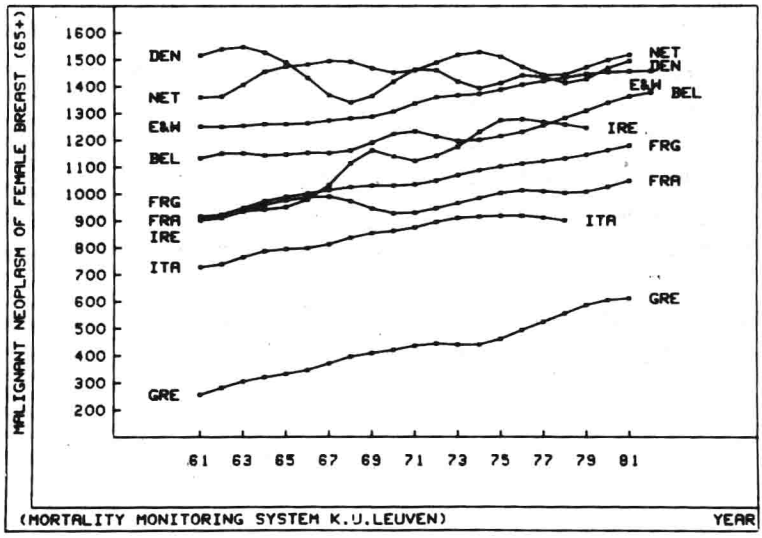

Fig. 5. Breast cancer mortality trends in nine Common Market countries (death rates per million, age adjusted 65+ years).

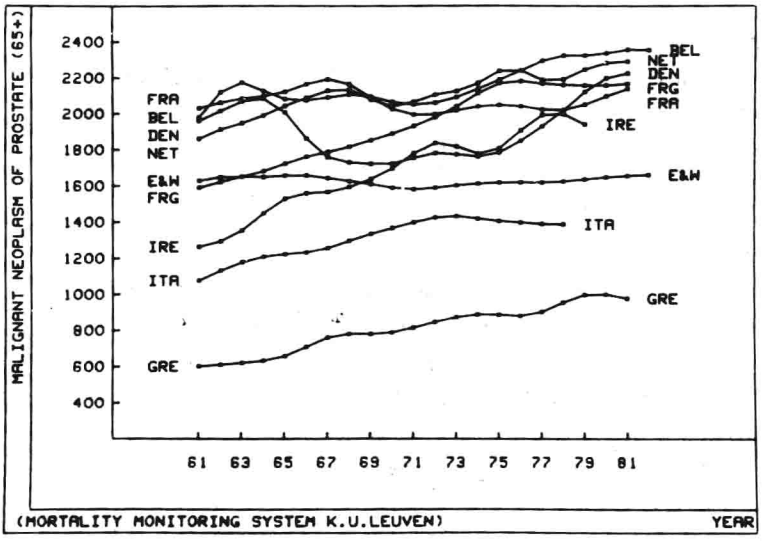

Fig. 6. Prostate cancer mortality trends in nine Common Market countries (death rates per million, age adjusted 65+ years).

figures 4 and 5 respectively. In middle-aged women breast cancer increased in all countries, with the exception of the Netherlands, where no significant change was observed. Whereas in general annual increases were moderate, i.e. about 1-1.5 %, a marked increase was observed in Greece, i.e. 4.6 %. In older women the same pattern was observed: increases in all countries but one (i.e. Denmark), ranging from 0.3 % in the Netherlands to 4.0 % in Greece.

Figure 6 shows prostate cancer mortality trends in older males. In six countries out of nine significant increases were observed, ranging from 0.7 to 2.6 %. No significant changes were found in Denmark, France, and England and Wales.

The number of deaths from total cancer and from sex-related cancers are given for 1978 in the Common Market as a whole and in Belgium (Table IV).

TABLE IV
NUMBER OF DEATHS FROM SEX-RELATED CANCERS IN THE COMMON MARKET AND BELGIUM IN 1978

Site	Common Market	Belgium
All malignant neoplasms (males)	347348	15455
Malignant neoplasm of prostate	28122 (8.1 %)	1426 (9.2 %)
All malignant neoplasms (females)	280599	11366
Malignant neoplasm of female breast	48568 (17.3 %)	2273 (20.0 %)
Malignant neoplasm of cervix uteri	7430 (2.6 %)	246 (2.2 %)
Malignant neoplasm of corpus uteri	13063 (4.7 %)	423 (3.7 %)
Malignant neoplasm of ovary		607 (5.3 %)

There are interesting relations between average rates of breast and prostate cancer mortality in both the 45-64 and the 65+ age group, confirming previous findings (2). Figure 7 shows this relationship for the latter age category. Average mortality rates of female breast and prostate cancer were found to be highly correlated ($r=0.79$, $p<0.001$). This relationship was checked by also looking at trends in both mortalities (Fig. 8). Again a significant correlation was obtained ($r=0.51$, $p<0.01$). It is remarkable that countries with low death rates for breast and prostate cancer have high changes in mortality and vice versa (compare Fig. 8 with Fig. 7). This suggests that the factors responsible for high mortality rates are relatively stable when high levels of these factors are prevalent. On the other hand, in countries with low levels these factors

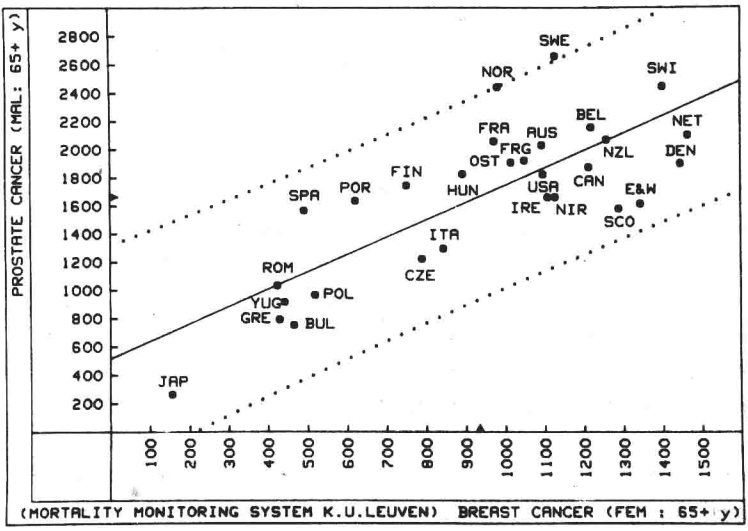

Fig. 7. Between countries relationship of breast and prostate cancer (death rates per million, age adjusted 65+ years, averaged over the period 1961-latest available year; n=29, r=0.79, p<0.001).

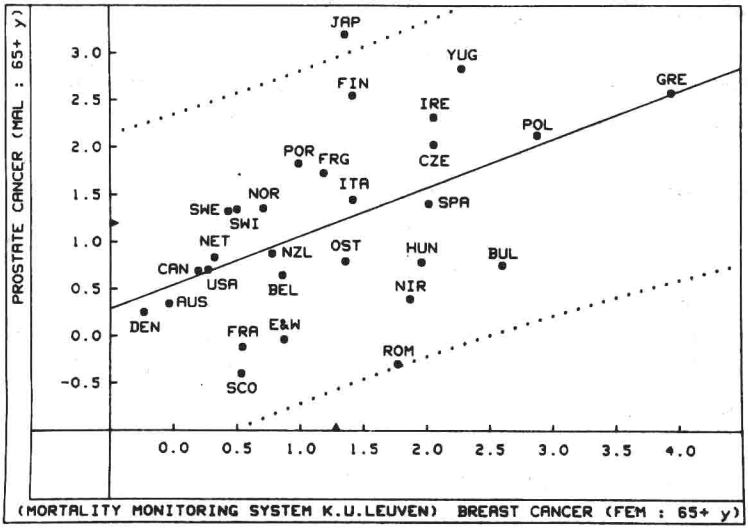

Fig. 8. Between countries relationship for annual changes in mortality of breast and prostate cancer (see methods; n=29, r=0.51, p<0.01).