"Pregnancy Related Risk Factors in Female Breast Cancer"

P.S.Carroll
UK

Summary

It is known that induced abortions have a different hormonal impact on cell development from full term pregnancies so that there are different consequences as regards the subsequent risk of breast cancer for women.

This paper reports analysis of data on Breast Cancer incidence from Great Britain and other European countries Sweden, Finland and the Czech Republic in relation to national trends in Abortion and Live Births.

It is found that birth cohorts of women in Great Britain and in Sweden and in the Czech Republic who have been exposed to higher abortion rates do have higher breast cancer incidence with a high measure of correlation. There is also negative correlation with Fertility in Great Britain where the cohorts of women who have had fewer children also have more breast cancer.

A simple regression model was fitted with response variable the cumulated cohort rate of breast cancer incidence within the age range 45 to 49. The cumulated cohort rates of Abortion and Fertility are treated as explanatory variables.

The same model was fitted to data for England & Wales and to data from Scotland. Predictions using this model suggest that the increase in breast cancer will continue at a higher rate in England and Wales than in Scotland. The difference is attributed to the lower abortion rate in Scotland.

For the years of abortion incidence 1968 to 1999 the abortion rate was decomposed into the nulliparous abortion rate and the parous abortion rate for England & Wales and Scotland. For Sweden this was done for the years from 1975 to 2000. The trend in nulliparous abortions was examined. It is thought that nulliparous abortions are more carcinogenic. If allowance is made for that, the modelling suggests a more rapid increase in breast cancer rates because of the more marked increase in nulliparous abortions among the cohorts of women reaching age 50 in the years 2000 to 20020.

Observed rates of Abortion, Nulliparous and Parous, and Fertility in Great Britain are expected to result in an increased female breast cancer incidence in future years by over 2% in England & Wales but by around 1.4% in Scotland currently and over future years to 2027.

"Facteurs de Risque d'incidence de Cancer du Sein liés à la Grossesse"

P.S.Carroll
UK

Résumé

On sait que l'avortement provoqué a un impact hormonal sur le développement cellulaire différent de celui de la grossesse menée à terme, d'où des conséquences différentes en ce qui concerne le risque subséquent de cancer du sein chez la femme. L'allaitement maternel et l'utilisation de contraceptifs hormonaux sont également envisagés comme facteurs de risque. L'âge à la première naissance et l'absence d'enfants sont de plus étudiés en ce qui concerne l'Angleterre. Cette contribution rend compte de l'analyse des données britanniques, qui comprennent des données pour les deux entités: Angleterre/Pays de Galles, et Ecosse, concernant l'incidence du cancer du sein par rapport à l'avortement et aux naissances vivantes, dans des cohortes d'années de naissance successives de femmes. On établit aussi des comparaisons, en utilisant des données suédoises, finlandaises et tchèques.

En définissant l'incidence du cancer du sein comme variable dépendante, et les facteurs liés à la grossesse comme variables explicatives, on établit un modèle d'analyse régressive linéaire. En utilisant ce modèle, on établit des prévisions pour l'incidence future du cancer du sein dans les années à venir.

PREGNANCY RELATED RISK FACTORS IN FEMALE BREAST CANCER

1. BIOLOGICAL MECHANISMS, MODELS AND ETIOLOGY, AVAILABLE STATISTICS

1.1 Pregnancy Related Factors Most Relevant.

"Most of the known risk factors relate to a woman's reproductive history" [Quinn M. et al. 2000] and "Several reproductive factors are associated with risk of breast cancer" [Swerdlow et al. 2001]. It seems that a woman who starts giving birth to children with a full term pregnancy at a young age and who has several children thereby improves her chances of escaping breast cancer later. But childless women and women who have induced abortions are at greater risk of breast cancer. Though the literature is sparse which shows lactation or breast feeding is a protective factor against breast cancer, this seems to be the opinion of most researchers.

Though some researchers and medical experts well acquainted with the biology of breast cancer say there is no difference between pre-menopausal breast cancer and post-menopausal breast cancer, in the UK there is emphasis on the distinction. "There are indications of differences in aetiology between breast cancers occurring before and after the menopause" and in respect of the trend in incidence in British breast cancer there is "a considerable continuing increase at the postmenopausal ages and a less marked, less consistent increase at premenopausal ages."[Swerdlow et al.2001]. The continuing rising trend in breast cancer incidence is more apparent at the post-menopausal ages in the countries considered while incidence rates at the younger ages remain low and show only small increases.

Age at menarche and age at menopause are reported in the literature as risk factors affecting breast cancer incidence. But the observed pattern of incidence in these variables does not a show any continuing trend to which the increase in female breast cancer might be linked in the countries considered. Young age at menarche is a positive risk factor. There was a trend to younger age of menarche but "the trend in age at menarche may have reversed for women born since the mid-1950s".[Swerdlow et al. 2001]

Certain medical treatments with a hormonal content are also risk factors. "Most of the known risk factors for breast cancer relate to a woman's reproductive history, and exogenous hormones, particularly oestrogen, probably also influence risk." [Black R et al. 2000] Hormonal contraceptives are known to be a positive risk factor. The decline in fertility in European countries since the 1960s is no doubt associated with the widespread use of these contraceptives. Some implicit allowance for their use may therefore be understood when declining fertility is modelled as an increasing risk factor.
There is no allowance, implicit or explicit, for hormone replacement therapy which is also known to be a positive risk factor.

1.2 Available Incidence Statistics.

Since 1971 it is thought that national data from 1971 onwards is reliably complete as regards cancer incidence in Great Britain including Scotland and England & Wales. For certain other European countries including Sweden and the Czech Republic there is also considered to be complete registration of newly diagnosed cancers. Duplicate registrations, which could make registration data erroneous, of new cancers are also thought to be less than 1% in Great Britain [Swerdlow et al. 2001]

It is the practice in Great Britain to reregister benign Carcinomas in Situ as Malignant cancers when they are reassessed as Malignant. In contrast the practice in the Czech Republic is not to do so. Hence the statistics in the two countries are not exactly comparable without making allowance for this artefact. Practice in Sweden is similar in this respect to the UK. When a cancer, first reported as benign, is reclassified as malignant after more than one year in Sweden it is registered again.

In this paper the ONS (Office for National Statistics in London) convention is followed in that incidence rates are computed using only the malignant cancers.

1.3 Age at First Birth

The Link Established with Age at the Birth of First Child which leads to Increased Risk of Subsequent Breast Cancer.

L. Lipworth et al. in the International Journal of Cancer (1995) [Lipworth et al.1995] discuss the etiology: "While there seems to be wide agreement that estrogens are involved in the etiology of breast cancer [Henderson et al. 1993], there is uncertainty as to the precise estrogenic environment that modulates the risk and the degree to which several reproductive risk factors are mediated by this mechanism. The pattern of increasing risk with increasing age at first term pregnancy [Mac Mahon et al. 1970] has been attributed to the extended duration of the interval when undifferentiated mammary stem cells are more likely to be susceptible to initiating carcinogens." Animal studies tend to support the hypothesis that a full term pregnancy decreases the lifetime risk among parous women due to terminal cellular differentiation of the mammary glands [Russo & Russo 1992]. However the short term effect of a full term pregnancy is to increase breast cancer risk [Lambe et al. 1994]. It is possible that the hormonal changes associated with a full term pregnancy, such as increased estradiol and progesterone levels, exert a transient adverse effect, which is later replaced by the long term protective effect of pregnancy.

On this principle a woman giving birth to a child at age 19 would benefit from ten years more protection of this kind than a woman whose first birth is at age 29. Hence the breast cancer incidence is less among those who are mothers at age 19, according to this model.

1.4 Pregnancy Terminations also a Risk Factor leading to Increased Breast Cancer Incidence.

As regards the effect of pregnancy terminations the same study [Lipworth et al. 1995] says "Given the established influence of the number and timing of completed pregnancies on a woman's risk of breast cancer [MacMahon et al.1970], it is reasonable to consider the extent to which risk may be affected by early terminated pregnancies. During the first trimester of pregnancy, free estradiol levels rise rapidly beyond peak levels usually experienced over normal ovulatory menstrual cycles [Howe et al. 1989]. Interruption of a pregnancy may accordingly increase the risk of breast cancer through an estrogen-mediated increase in breast cell proliferation rates during a critical period and the absence of a terminal differentiation effect brought about by a full term pregnancy."

This study [Lipworth et al.] goes on to state: "Epidemiological evidence regarding the relationship between breast cancer and spontaneous abortion is inconsistent, with several reports suggesting an increase in risk and others finding an inverse or no association. a few studies have reported a substantially elevated risk of breast cancer among women experiencing a first trimester abortion, whether spontaneous or induced, prior to the first full-term pregnancy or at a young age."

1.5. Abortion Recognised as a Risk Factor.

Mads Melbye et al. in The New England Journal of Medicine [Melbye et al. 1997] recognise such models for factors influencing this risk:

"Background. It has been hypothesised an interrupted pregnancy might increase a woman's risk of breast cancer because breast cells could proliferate without the later protective effect of differentiation." [Melbye et al. 1997]

"A full-term pregnancy increases a woman's short-term risk of breast cancer, possibly as a result of the growth-enhancing properties of pregnancy -induced estrogen secretion. By contrast, such a pregnancy decreases the long term risk of breast cancer, perhaps by inducing terminal differentiation of the susceptible mammary cells. [Daling et al.] Studies in animals suggest that the potential for terminal differentiation of breast cells is lower from a pregnancy terminated by abortion than for a full term pregnancy. On this basis Russo & Russo [Russo & Russo 1992] have proposed that a full term pregnancy allows complete differentiation of breast cells, thereby protecting against cancer, whereas abortion forestalls the late protective effect of differentiation thereby increasing the risk of breast cancer." [Melbye et al. 1997]

1.6. Early Abortion a Particular Risk Factor.

Of particular interest in a British context is the suggestion that early abortion before a full-term pregnancy leads to a particular increase in the risk of breast cancer. M.C. Pike et al.British Journal of Cancer 1981 [Pike et al.1981] reported "A first trimester abortion before a first full-term pregnancy, whether spontaneous or induced, was associated with a 2-4 fold increase in breast cancer risk."

This fits in with what is known of the etiology of breast cancer. "Our finding makes biological sense if one considers breast tissue as merely proliferating in early first pregnancy; the protective effect of first full-term pregnancy is then brought about by a combination of cell differentiation and possible permanently altered hormone levels." [Pike et al.]

These findings were reinforced by a subsequent study by O.C.Hadjimichael et al. British Journal of Cancer 1986 "Among women with one live birth at the time of cohort identification, a spontaneous abortion before this live birth was associated with a 3.5 fold increase in breast cancer." [Hadjimichael et al.1986] The result was clear enough, though the number of cases was small, and a biological explanation is also plausible. "In summary, these data indicate that an abortion prior to the first live birth may increase a woman's risk of breast cancer. Whether this is a result of incomplete development of the mammary gland due to the interrupted pregnancy or of a hormonal imbalance that may result in both the spontaneous abortion and the cancer of the breast, or of some unsuspected factor, it is clear that further exploration of this issue is warranted."[Hadjimichael et al.1986]

This last study was concerned with spontaneous rather than induced abortion. Research with representative samples of women who have had induced abortions is more difficult because of the possibilities of such biases as caused by "recall and response" errors. Women who have had induced abortions may be more reluctant to participate in such studies and if they do they may not declare the history of induced abortion.

1.7. Induced Abortion a particular Risk Factor.

It is possible that an induced abortion, which tends to take place later than a spontaneous abortion, is more damaging to the development of breast cells and could have a more severe hormonal impact that leads to a greater risk of breast cancer. Inducing abortions in animals, with variation of the gestational ages, might be a means of investigating this question. But there could also be ethical difficulties here as such experiments would involve some cruelty to animals.

1.8. A Second Trimester Induced Abortion could be More Damaging than a First Trimester Spontaneous Abortion.

It is said in early pregnancy oestrogen levels soar and cause breast cells to proliferate. In later pregnancy the woman's progesterone 'organises' these cells so that they can secrete their milk. But if this pregnancy is aborted, this later stage cannot take place and the proliferated breast cells become vulnerable to cancer.

Other writers say the induced abortion leaves the breast tissue vulnerable and susceptible to carcinogens [Kelsey 1989, Somerville 83].

1.9 The Current Debate.

There is controversy as to the effect of induced abortions as a risk factor affecting Breast Cancer among women. There is a substantial literature on the subject in the medical journals. The paper by Joel Brind et al. [Brind et al.1996] surveys 33 published reports in a meta-analysis. The findings "support the inclusion of induced abortion among significant independent risk factors for breast cancer".

A well established epidemiological finding on breast cancer among women, that is now beyond dispute, is that early parity i.e. having a full term pregnancy such as giving birth to a liveborn child at a young age gives some protection against breast cancer later. [Leon 1988]

The state of interrupted hormonal development consequent on an induced abortion also leaves a woman more vulnerable to breast cancer in later years.

2. Breast Cancer in a British Context.

2.1 Screening. Registration. Abortion as a Risk Factor.

The United Kingdom is notable for a high incidence of breast cancer compared to other countries. There is said to be as high a risk as 1 in 6 that a British woman contracts this disease. The importance of the disease has been recognised and the British screening programme for breast cancer is well developed and is considered to be thorough and comprehensive. It started around 1989 and by 1993 is considered to have covered all the country. It has itself led to an increase in cancer incidence being recorded in that cancers that might previously have been undetected are now being detected.

Besides an impressive screening programme for female breast cancer there is in Great Britain a system of cancer registration, for all cancers. This can be linked to the National Longitudinal Study which covers one or two per cent of the population. Like the Longitudinal Study, the Cancer registration system uses name and date of birth to identify persons and the new cases of cancer are collated first by the Regional Health Authorities and later the national data for the two jurisdictions England & Wales (Wales now separately) and Scotland are aggregated.

The Social Distribution of Cancer 1971-75 by D Leon, Longitudinal Study No 3 HMSO 1988 [Leon 1988] used this linking of records of cancer registration and the records of the census and births and deaths that are included in the Longitudinal Study. The SRRs or Standardised Registration Ratios for breast cancer show a J-shaped pattern with age at birth of first child. But there was also found that the lowest SRRs were for women having three or more children. Multi-parity was found to have an additional protective effect beyond that of age at first birth. These findings using cancer registrations in 1971 to 1975 were little affected by legal abortions after 1967.

The official British publication on Cancer [HMSO 1994] does not mention Abortion explicitly in the chapter on Breast Cancer but considered that the risk factors were mainly in women's reproductive history. This might be understood as an implicit reference to abortion. "The majority of known risk factors relate to a woman's reproductive history, and it seems highly probable that hormones, particularly oestrogen, play an important role in the development of breast cancer. None of them is amenable to prevention, although women planning to have children should be informed of the effect of age at first birth." Perhaps this also implies that women contemplating having an abortion should be informed of the increased breast cancer risk implied. Even if it were the case that the process of interrupting the pregnancy does not itself make her more vulnerable to breast cancer she is missing the chance to have a first birth at a younger age that the abortion will prevent. As pointed out in a 1998 paper [Carroll 1998], there is in Great Britain a concentration of abortions at young ages and most women having an abortion in Great Britain have not yet given birth to a Live Child.

Abortions are registered in Great Britain but not linked to the Longitudinal Study or to the system of Cancer Registration. Because abortions take place in Great Britain at an especially young age of women and the risk of breast cancer become substantial only after age 45 or age 50 the influence on breast cancer of abortion is taking some time to establish. The lack of facility to link abortion into the Longitudinal Study is making future research on breast cancer using the LS vulnerable to confounding between abortion and other variables such as age at first birth, number of children and childlessness. A cohort approach using correlational data seems most promising.

2.2. Trends in British Breast Cancer Incidence. England & Wales. Distribution by Age of Women. Trend over Recent Years. Published figures with quinquennial age groups.

The published data for breast cancer incidence in England & Wales is by quinquennial age groups. Figure 1 shows the trend over the years 1971 to 1997 in England & Wales in respect of the changing incidence for certain age groups of women 40-44,45-49 and 50-54.

All age groups 40 to 54 show some increase. For the age group 50-54 this is of course influenced by the screening programme that operated nationwide from 1989. In 1993 there was a drop in incidence at the later part of this age range and this may be because the cancers that would have been manifested without screening were already discovered. But increases in incidence since 1993 are not attributable to screening. Also apparent is the higher rate of increase in post-menopausal cancer over the epoch.

2.3 Abortion Incidence in Great Britain. England & Wales and Scotland.

Since the implementation of the 1967 Abortion Act in Great Britain legally induced abortions have increased. The age specific rates in England & Wales are compared in Figure 2 for 1989 and 1999. The abortion rates in England & Wales (resident women) have risen at each age in 1999 since 1989. The adult rates have increased more significantly. The peak or modal age is now around age 19-20.

Total Abortion Rates, TARs that are the sum of the age specific rates for a particular year, are compared between England & Wales and Scotland in Figure 3 over the years from 1968 to 1999. The total abortion rate in England & Wales is now around 0.5 (slightly increasing to .51 in 2000) and that in Scotland is around 0.35. The lower rate in Scotland is attributed to more traditional and Christian values being maintained there among a larger proportion of the population.

2.4 Risk Factors examined in relation to Breast Cancer Incidence. England & Wales.

Cumulated Cohort Rates of Breast Cancer Incidence in England & Wales. Comparison with cumulated abortion Rates, the mean age at first birth of parous women, nulliparity and completed cohort fertility (average number of children).

For England & Wales single year of age data on breast cancer incidence is available from ONS in the form of number of new cancers each year from 1971 to 1997. Age specific rates can then be derived using official mid-year population estimates for the female population. Summation of these rates across the diagonals of the matrix then produce cumulated cohort rates for successive birth cohorts. For Birth Cohorts born in years from 1926 up to 1948 the total incidence data within ages 45 to 49 is complete. This is plotted in Figures 4-7 against known explanatory variables that have been found to influence breast cancer incidence.

Figure 4 shows Cumulated Breast Cancer incidence within ages 45 to 49 against the cumulated abortion rates. Legal abortions were virtually zero before 1968. There is a high positive correlation between these two variables as expected (correlation coefficient 0.84). Those born in 1947 are thought to have been most affected by pre-1968 unregistered (illegal) abortions and the dip in the cohort abortion rate for that year of birth reflects this.

Figure 5 shows the trend in Mean Age at First Birth in relation to Breast cancer in the same age range for the same birth cohorts. When it is so well established that a full term pregnancy at an early age provides strong protection against breast cancer later it is surprising to have high negative correlation (correlation coefficient -0.775). This seems to have been an unusual epoch in history in which female breast cancer incidence increased among women who first gave birth to children at a younger age. Because of this anomaly it is not proposed to use this variable as an explanatory variable in modelling.

Figure 6 shows the trend of this cancer incidence over successive birth cohorts against childlessness. Again there is an anomaly. Breast cancer has increased while childlessness has decreased over the same epoch. There is some negative correlation (coefficient -0.53). It is not proposed to use childlessness as an explanatory variable for modelling.

Figure 7 shows the trend of this cancer incidence against total fertility (average number of children born to women in the cohort). Here there is some negative correlation as expected (correlation coefficient -0.3) which is most apparent in more recent cohorts.

2.5 MODELLING England & Wales.

A simple regression model was fitted using the 23 years data for birth cohort cumulated rates for England & Wales. Breast cancer incidence within ages 45 to 49 is the response variable Y. The two explanatory variables are X1 cumulated abortion incidence and X2 cumulated fertility.

The fitted model $Y_i = a + b_1X_{1i} + b_2X_{2i} + error_i$
where a is a constant and b1 and b2 are constant coefficients,
was a simple additive fixed effects model with no weighting and no transformations. It is assumed accordingly that breast cancer incidence is simply proportional to a combination of

abortion and no of children.

The fitted model showed an R-squared 0.94 (multiple correlation coefficient 0.96). The coefficients were b1 for X1 .0089 (95% confidence interval .00741 to .01) and b2 for X2 -.0027(95% confidence interval -.0035975 to -.0018122) with constant term .01316.

2.6 FORECASTING using the Model. England & Wales.

The present total abortion rate TAR for England & Wales is around 0.52 and the present total Fertility Rate TFR is around 1.66(provisional estimates for 2000) . Entering these into the model gives a forecast cohort incidence of breast cancer in the future assuming these rates continue unchanged so that they become the future cohort rates. This shows an increase to 0.01328 for cohort incidence of breast cancer, within the age range 45 to 49, compared to the last rate shown for cohorts born in 1948 at .0092. This represents a 44.39% increase over a period of 30 years to 2027, equivalent to an annual increase of 1.2% compound which is similar to what has been experienced in the recent past in England & Wales.

2.7 Nulliparous and Parous Abortion Rates.

When the 1967 Abortion Act came into force in Great Britain most abortions were performed on Parous women who had previously given birth to a live born or still born child. This pattern changed as shown in Figure 8 so that in the 1980s near to 60% of abortions were carried out on nulliparous women, with no previous full term pregnancy. More recently the proportion on nulliparous women in the 1990s has been around 53%.

Figure 8 was constructed using published data in the annual Abortion Statistics publications of ONS. For years 1968 to 1980 single year of age data was published showing numbers of abortions for all women and also for women of 0 parity. For both rates the same denominator, number of the female population at mid-year of that age, was used. For years 1981 to 1999 the published data was grouped in quinquennial age groups and the single year of age data was estimated using Scotland and earlier years in England & Wales as a pattern for the distribution within the quinquennial intervals. There is some bias in the data as used in that for some years there were relatively large numbers (a few thousand in some years in the 1980s) of cases where parity was not declared. The convention has been followed that these women are treated as having non zero parity and consequently there is some underestimation of the nulliparous rates for some years. This does not apply to recent years where only a few cases of women not declaring their parity are recorded.

2.8 Cohort Nulliparity and Implications for Estimation.

The cumulated cohort rates for both Nulliparous and Parous abortions were calculated and are shown in Figure 9. Abortion data is incomplete for women born since 1955. But the higher rates of nulliparous abortions even for these more recent cohorts are already apparent.

The steep rate of increase is evident for women born in the 1950s approaching age 50 in the years 2000 to 2010 is shown, less than .1 for those born in 1950 and more than .2 for those born in 1960. If nulliparous abortions are much more carcinogenic there will be a correspondingly steeper rate of increase in breast cancer for women in that age in the years to 2020. When an appropriate weighting is introduced into the regression formula in section 2.6, with a multiplier applied to the coefficient of abortion, we find there is expected a 98% increase over 30 years and this is equivalent to 2.2% per annum compound. If this accelerated rate of increase is observed in new breast cancer registrations henceforth it can be attributed to the influence of nulliparous abortions.

2.9 Scotland.

Breast cancer incidence rates for Scotland are available from the ISD Information and Statistics Division office of the National Health In Scotland in Edinburgh by single years of age from 1971 up to 1997. But the Scottish rates for Childlessness (Nulliparity) and Mean Age at First Birth of parous women are not available.

Figure 10 shows the trend in Breast Cancer incidence within ages 45 to 49 for successive birth cohorts of women born from 1926 to 1948 and the corresponding completed cohort abortion rates. The pattern is similar to that shown above for England & Wales. Historically Scotland has reported slightly higher incidence of female breast cancer in past years since 1971. But the recent increase has been less in Scotland than in England & Wales.

Figure 11 shows the same trend in breast cancer incidence compared with the trend in completed cohort fertility for Scotland. Fertility has been slightly higher in Scotland than in England & Wales throughout the period considered for female birth cohorts in Scotland born from 1926 to 1944. But more recently it has fallen significantly below that in England & Wales so that the Government Actuary now uses a lower fertility rate for Scotland in official population projections.

Figure 12 shows for Scotland the trend in breast cancer incidence for women within the age groups 40 to 44, 45 to 49 and 50 to 54. The comparison with Figure 1 for England shows that the increase in incidence has been greater in England than in Scotland in more recent years.

2.10 Model for Scotland.

A similar model was fitted for Scotland for the last 15 years of birth cohorts born from 1934 to 1948:

Y = a + b1X1 + b2X2 + error,
where Y is the breast cancer incidence response and X1 is the cohort abortion cumulated rate and X2 the average number of children.

Here a = .0112123
b1 = .0062416(95% confidence interval -.0166021 to .0290853) and
b2 = -.013695(95% confidence interval -.0050144 to .002275) as fitted. The R-squared

is 0.6786 (multiple correlation coefficient .824).

2.11 Future Projections for Scotland.

The present total abortion rate TAR for Scotland is around 0.37 and the present total Fertility Rate TFR is around 1.5. Entering these into the model as X1 and X2 respectively gives a forecast cohort incidence of breast cancer in the future assuming these rates continue unchanged so that they become the future cohort rates. This shows an increase to 0.01134 for cohort incidence of breast cancer, within the age range 45 to 49, compared to the last rate shown for cohorts born in 1948 at .0092. This represents a 23.29% increase over a period of 30 years to 2027, equivalent to an annual increase of 0.7% compound which is similar to what has been experienced in the recent past in Scotland.

Lower abortion rates in Scotland can be expected to lead to lower breast cancer incidence rates than in England. And this influence is only partly offset by the expected lower fertility in Scotland.

2.12 Comparison between Scotland and England & Wales: Breastfeeding.

Whereas the fitted model makes sense when fitted separately to England & Wales and to Scotland there remain two puzzling questions: why did the Scottish women in the earlier cohorts considered have more breast cancer than their English contemporaries when they had more children and fewer abortions? and why is the coefficient of fertility in the model fitted for Scotland so small?

Consideration of Breast Feeding may provide at least some partial explanation of these differences.

"The breast feeding rate in Scotland is the second lowest in Europe, with 55% of women breastfeeding at birth." [Britten et al. 2001] In particular it is lower than the rate of breast feeding in England. As a result it seems that Scottish women when they do have children do not get as much protection from breast cancer later as would be expected from their higher fertility.

The trend over time also shows that this difference was even higher in the earlier years of the epoch considered.

Breastfeeding in the United Kingdom 1995 [Foster & Lader ONS 1997] reported a trend since 1980 in Breastfeeding Initiation Rates:

	1980	1985	1990	1995
	%	%	%	%
England & Wales	66	65	64	68
Scotland	50	48	50	55

The rates shown refer to the proportion of babies breast fed at birth. In the years in the 1960s and 1970s before 1980 it is probable that Scottish rates were even lower. Through much of the period considered, rising incidence of breast feeding in Scotland has therefore run parallel to the decline in the Scottish birth rate and perhaps to some extent offsetting its effect as a risk factor in breast cancer. In this way the rather small coefficient of fertility for Scotland in the fitted model can be partly explained.

2.13 Nulliparous and Parous Abortions in Scotland.

Figure 13 shows the trend. It is based on data supplied for exact single years of age for all years from 1968 to 1999 by the Information and Statistics Division of the National Health in Scotland. The convention is also followed here that where parity is not declared by the woman having an abortion she is treated as Parous. The resulting bias is thought to amount to a small error of underestimation of the resulting Nulliparous Abortion Rate in Scotland. The pattern is broadly similar to that for England & Wales in Figure 8 with the lower abortion rates applicable to Scotland. But in the 1970s the proportion of nulliparous abortions was lower in Scotland than in England. After 1983 most abortions have been carried out on nulliparous women in Scotland.

The cumulative cohort rates of Parous and Nulliparous Abortions are shown in Figure 14. As with England & Wales there is a steep increase in the cumulated rate of Nulliparous abortions on the part of women approaching age 50 after the year 2000. As a result an accelerated increase in breast cancer incidence can also be expected. Making a weighting adjustment to the coefficient of abortion in the regression formula in 2.11 suggests that an increase in breast cancer over 30 years of 50.4% can be expected. This amounts to an annual rate of increase of 1.37%.

3.1. Sweden. Breast Cancer Incidence in Sweden.

Breast Cancer Incidence rates were supplied by The National Board of Health and Welfare's Centre for Epidemiology in Stockholm for single years of age both for all abortions and for nulliparous abortions for all years from 1975 to 1999. Three missing years were estimated from published data for those years in quinquennial age groups. Figure 15 shows the comparison between Sweden and Scotland over the years 1960 to 1996 of incidence within the age group 45 to 49. The increase in incidence is comparable to what has been noted in Great Britain. However it should be noted that breast cancer screening is widespread in Sweden for females in the age range 40-49. The relative increase in Sweden since the late 1980s is partly to be explained as a consequence of this. For 1997, the last year shown, the rates are very close in both countries and to the rate for England & Wales. Perhaps the effect of higher rates of abortion in Sweden are offset by the effects of more breast feeding in Sweden compared to Scotland, so that the net current effect is to produce similar rates of incidence.

Figure 16 shows the comparison between Scotland and Sweden for incidence within the age range 50-54. Here the trend is shown to be very similar in both countries. Screening for breast cancer operates in both for this age range. Most recently the rates in Scotland have been higher in this age range. Perhaps to a small degree this is due to the effect of screening in Sweden and no screening in Scotland in the previous age range below age 50 means that new cancers that might be discovered before age 50 in Scotland are now discovered after age 50 and this produces a relatively high rate of new cancers discovered in this age group in Scotland. There was a larger decline in Fertility in Scotland than in Sweden for birth cohorts born later in the 1940s as shown comparing Figures 11 for Scotland and 20 for Sweden and this is presumably one explanation for the higher Scottish rate of breast cancer incidence.

3.2. Abortion in Sweden.

The high abortion rate in Sweden also tends to support the hypothesis that higher abortion rates in more recent cohorts have led to more breast cancer.

Figure 17 shows the comparison between Sweden and England & Wales in respect of the total abortion rates over the years 1975 to 1999. Swedish rates have been higher than in Great Britain over this time.

High abortion rates has been reported in Sweden since the 1970s. It declined until 1993 and has since risen slightly and in 1996 it was 0.556. The latest rate is for 2000 at .55, still higher than in England.

Of course other factors are also influencing the risks of breast cancer in Sweden. But a first analysis does suggest that high abortion rates in Sweden have led to higher breast cancer incidence rates. Swedish abortions are concentrated on younger women as shown in Figure 18, which compares the age specific rates in Sweden with those in England & Wales for 1999. But Figure 18 also shows Swedish women choosing abortions are not as young as English women having abortions. Below age 26 the English rate is higher than the Swedish rate. Possibly the higher rate of abortion in Sweden leads to less breast cancer because Swedish women who have had abortions are older and often have given birth to live children before having an abortion.

Figure 19 shows the cumulated cohort rate of Abortion versus cumulated rate of breast cancer within the ages 45-49. There is a high correlation between Abortion rates increasing and Breast Cancer rates also increasing over 22 years of birth from 1929 to 1950. But this needs to be viewed with some caution in that pre-1975 abortions were possibly significant in Sweden and are not included in the statistical data used.

Swedish fertility rates are broadly similar to those in Great Britain. But the trend of fertility by cohorts over the epoch considered shows positive correlation with breast cancer as shown by Figure 20 which plots the cumulated cohort rate of Fertility versus cumulated rate of breast cancer within the ages 45-49. The more recent cohorts in Sweden that have higher rates of breast cancer have also higher completed cohort fertility.
Unlike in Great Britain, a decline in fertility over the epoch has not been a contributing factor to more breast cancer. This also points to abortion as main cause of increasing breast cancer incidence in Sweden.

3.3 Modelling and Forecasting for Breast Cancer in Sweden.

As the last graphs in Figure 20 shows, there is an anomalous positive correlation between fertility and breast cancer incidence over this epoch. This makes fitting the same model as for Great Britain inappropriate. There is a particular anomaly over the most recent years of birth cohorts. The trend is to less breast cancer within ages 45 to 49 for those born in the years 1947 to 1950 even though they have had fewer children and more abortions in the more recent cohorts.

Figure 21 shows Nulliparous Abortion rates compared to Parous for the sequence of years from 1975 to 2000. For the last year 2000 the Nulliparous abortion rate has overtaken the Parous abortion rate. As in Great Britain during the earlier years when liberalised abortion law was introduced most abortions were carried out on women who already had children. Around 1985 the comparison between Figures 8 and 21 shows the nulliparous abortion rate in Sweden and in England was quite similar at around .22 in both countries.

Figure 22 shows cumulated cohort rates of Nulliparous and Parous abortions versus cumulated cohort rates of breast cancer within ages 45 to 49. The steep recent increase in Nulliparous abortion rates are likely to lead to an accelerated increase in Swedish breast cancer incidence rates when cohorts of women reach the age of post-menopausal cancer in future. For Sweden again it may be advisable to note that pre-1975 abortions are not recorded. If they were the growth in nulliparous abortion rates shown in Figure 22 might be more like a straight line.

As in England it seems that any accelerated rate of increase in breast cancer incidence observed henceforth may be the result of nulliparous abortions.

4. Finland.

Breast cancer rates for Finland have been supplied by the Finnish Cancer Registry. Breast cancer incidence in Finland has fully recorded for many years. The incidence rates for the age groups 40-44, 45-49 and 50-54 are shown in Figure 23.

Finland in the 1970s has shown something similar to the high abortion rates associated with the former communist countries of Eastern Europe. The trend to lower abortion rates is shown in Figure 24. The abortion rate in Finland is now even lower than that in Scotland (0.3 in 1997).

The high abortion rates in the late 1970s in Finland have been followed by high breast cancer incidence in Finland in the 1990s as shown in Figure 23. On this score some fall in breast cancer incidence is to be expected in Finland in the future as a consequence of lower abortion rates.

5. The Czech Republic.

5.1 Official Statistics, Breast Cancer, Abortion and Fertility.

The Czech Republic has had especially good recording systems for national demographic and health data. A former communist country that has had a high abortion rate in the communist era has now become more Westernised. Both cancer registration and abortion registration were thought to be complete and the incidence statistics reliable in the communist era.

The incidence data are as supplied by Health Statistics in Prague. Figure 25 shows breast cancer incidence trends of malignant breast cancers within age groups. There is a trend to increasing incidence and the pattern of increase is similar to what is shown in Figures 1 for England & Wales, Figure 12 for Scotland and Figure 20 for Sweden but the rates of incidence remain lower than in Northern Europe. It is recognised that breast cancer incidence is less in southern Europe and this seems also to apply to the Czech Republic.[Black R et al 2000]

Figure 26 shows the trend in abortion incidence since 1968 which has been high in the communist era. The abortion total figures for the years 1960 to 1968 have been published but the data is difficult to transmit electronically. The high rate in 1960 (67 550 legally induced abortions in 1960) suggests there were significant numbers of abortions even before 1960. Available abortions were largely free of charge. "This very particular "abortion culture" - in which abortion was commonly seen as a form of contraception - was encouraged by the absence of any moral or religious scruple on the part of the majority of the population. The rise in the number of abortions received an extra boost in the early 1980s with the introduction of vacuum aspiration technique (VAT), which was administratively simpler and posed fewer dangers to the woman's health. A further landmark in the development of abortion came in 1987 when a new abortion law came into force, abolishing the abortion commissions and giving women a basically unlimited right to decide the fate of their pregnancies." [Z Pavlik et al. 1996] Up to 1993 abortion statistics are thought to be complete. Since 1993 there appears to be some possibility that abortions are being done for cash without official registration and the decline in the abortion rate since then may be due to this factor as well as to the modern availability of other method of contraception now in the Czech Republic. Even the official abortion rate is stili somewhat higher in 1997 than the rate in England & Wales as shown in Figure 26.

Abortions took place in the Czech Republic mainly on women who are married and when they have already given birth to liveborn children. The age distribution is as shown in Figure 27. Whereas the peak age is at 20 in England & Wales in 1997, the modal age of abortion is 27 in the Czech Republic.

Figure 28 shows cumulated cohort breast cancer rates within ages 45 to 49 against cumulated abortion rates for each birth cohort born from 1932 to 1947. Again the gradient in cohort abortion rates would be less steep if abortions before 1968 were known in detail and included.

Figure 29 shows cumulated cohort breast cancer rates within ages 45 to 49 against fertility for each birth cohort. The pattern is broadly similar to that for England & Wales in Figure 7 and for Scotland in Figure 11. In the early 1970s alarmingly low fertility was experienced in the Czech Republic and good maternity benefits were introduced from 1975. This increased the birth rate and the cohort rates rose from year of birth 1943 to 1947 - see Figure 29. After the mid 1980s the benefits tended to be frozen and devalued by inflation. The birth rate is now very low in the Czech Republic(1.13 TFR in 1999)

Figure 30 shows that the proportion of nulliparous abortions has increased recently. This trend is parallel to the decline in the Czech birth rate now one of the lowest in the world at 1.12 in 1999. If nulliparous abortions are much more carcinogenic they will lead, in conjunction with the lower birth rate, to an increase in breast cancer to be expected in the future.

5.2 Breast Feeding in the Czech Republic.

The following table was supplied by IHIS Prague showing the extent of breast feeding in the Czech Republic in the 1990s.

% of Infants Breastfed

Year	1993	1994	1995	1996	1997	1998	1999	2000
till 6 weeks	38.4	37.2	38.2	39.7	34.5	29.7	27.5	26.0
6 weeks to 6 months	47.6	47.3	46.2	44.7	46.8	47.3	46.5	45.3
over 6 months	9.0	10.5	10.7	10.6	13.6	17.6	21.0	23.8

Table 5.2

By comparison with the comparable table for Great Britain in section 2.12 it is apparent that the initial rate of breast feeding is much higher in the Czech Republic. The duration of breast feeding also seems much longer in the Czech Republic.
The pattern and extent of breast feeding is understood to have been similar in the 1970s and 1980s in the Czech Republic. This seems to have been a factor in limiting the increase in breast cancer notwithstanding the high abortion rate.

6. Outlook.

Both in the British Isles and in continental Europe there is a sharply increasing completed cohort nulliparous abortion rate among those women approaching age 50. Assuming nulliparous are much more carcinogenic than parous abortions, an accelerated increase in breast cancer incidence will be experienced in the first years of the 21st century as a result of the high nulliparous abortion rates of the late 1970s and 1980s.

This applies to Sweden and also to England & Wales and Scotland. In the Czech Republic the increase in nulliparous abortions is more recent and the resulting increase in breast cancer incidence can be expected later. Very low fertility now experienced in the Czech Republic also points to an increase in breast cancer in future years.

Lower fertility is a parallel trend and a further risk factor leading to increased incidence of breast cancer to be expected in all European countries.

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Data for England & Wales on Breast Cancer Incidence and Abortion Incidence and the demographic data on Parity in England & Wales was supplied by the Office for National Statistics in London(Penny Babb, Clare Griffiths, Nirupa Dattani). For recent years since 1996 breast cancer incidence data for Wales came from the Welch Office, Welch Cancer Intelligence and Surveillance Unit in Cardiff(Dr John Steward).

Data on Scotland for Breast Cancer incidence and Abortion incidence in Scotland was supplied by the Information and Statistics Division of the National Health in Scotland(Veronica Harris and Ross Elder) and also some information on breast feeding in Scotland(Kate Wilkinson). Scottish demographic data on Parity and Completed Cohort fertility rates was supplied by the office of the Registrar General in Scotland in Edinburgh (Graham Jackson). Population data for England & Wales and Scotland came from the Government Actuary's Department and their 1998- based population projections(Steve Smallwood).

Swedish data came from Statistics Sweden (Clas Hedberg, Mrs Lotti Barlow, Gun Alm Stenflo, Shiva Ayoubi).

Data for Finland came in respect of breast cancer incidence from the Finnish Cancer Registry (Dr Eero Pukkala) and for Abortion from the National Statistical office STAKES.

In the Czech Republic data was supplied by the Health Ministry Statistics Department (Dr Jiri Holub, Zusanna Kamberska, Marie Jechova).

The computing was done by Nigel Koo Ng, Sangeeta Chopra, Denise Tuedt, Kate Jainchill and Josh Taylor.

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Figure 1
Average Yearly Rates of Incidence of Malignant Female Breast Cancer in England and Wales within Age Groups 40-44, 45-49 and 50-54 from 1971-1997

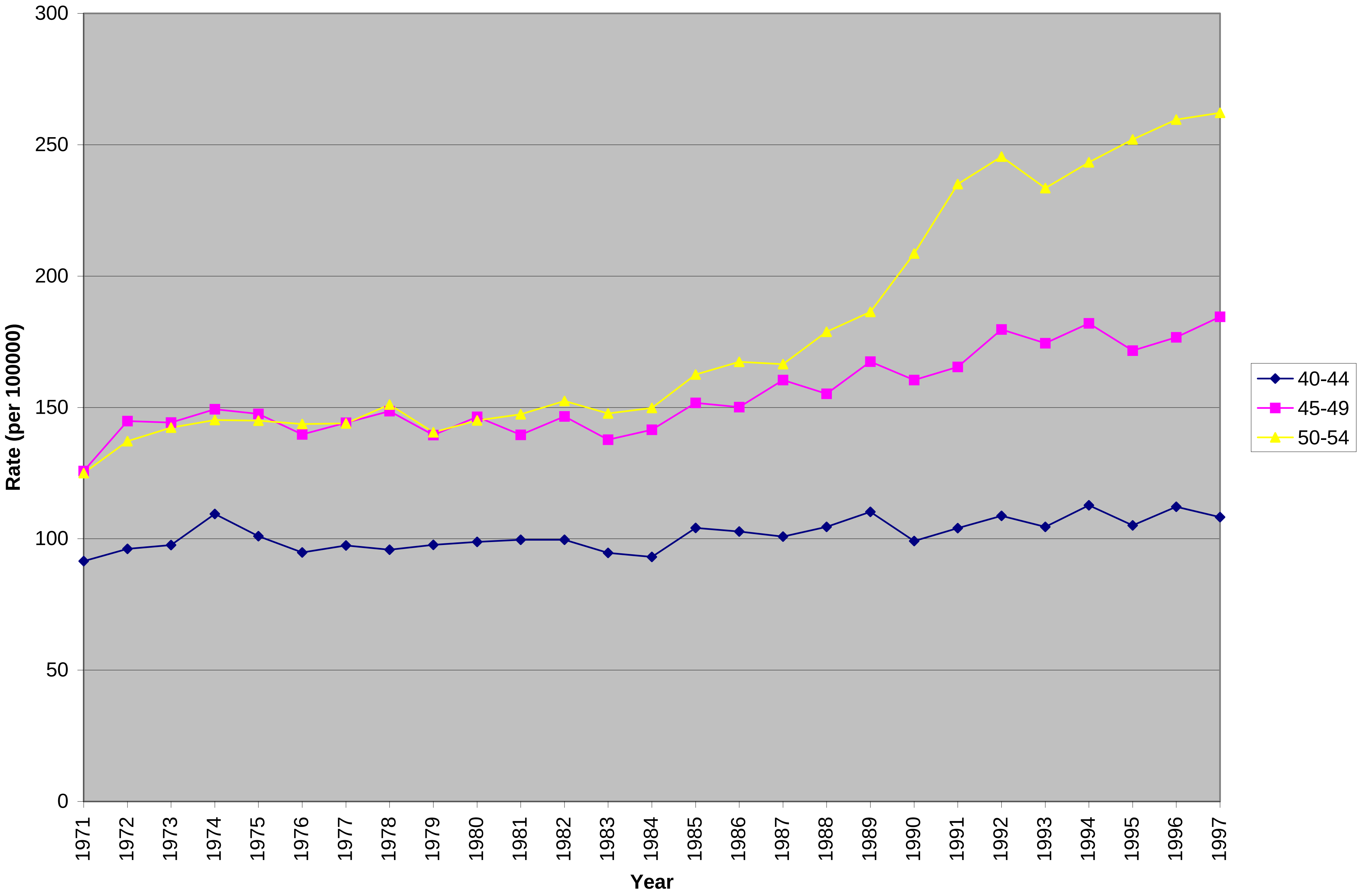

Figure 2
Abortion Rates of Resident Women for England and Wales 1989 vs. 1999

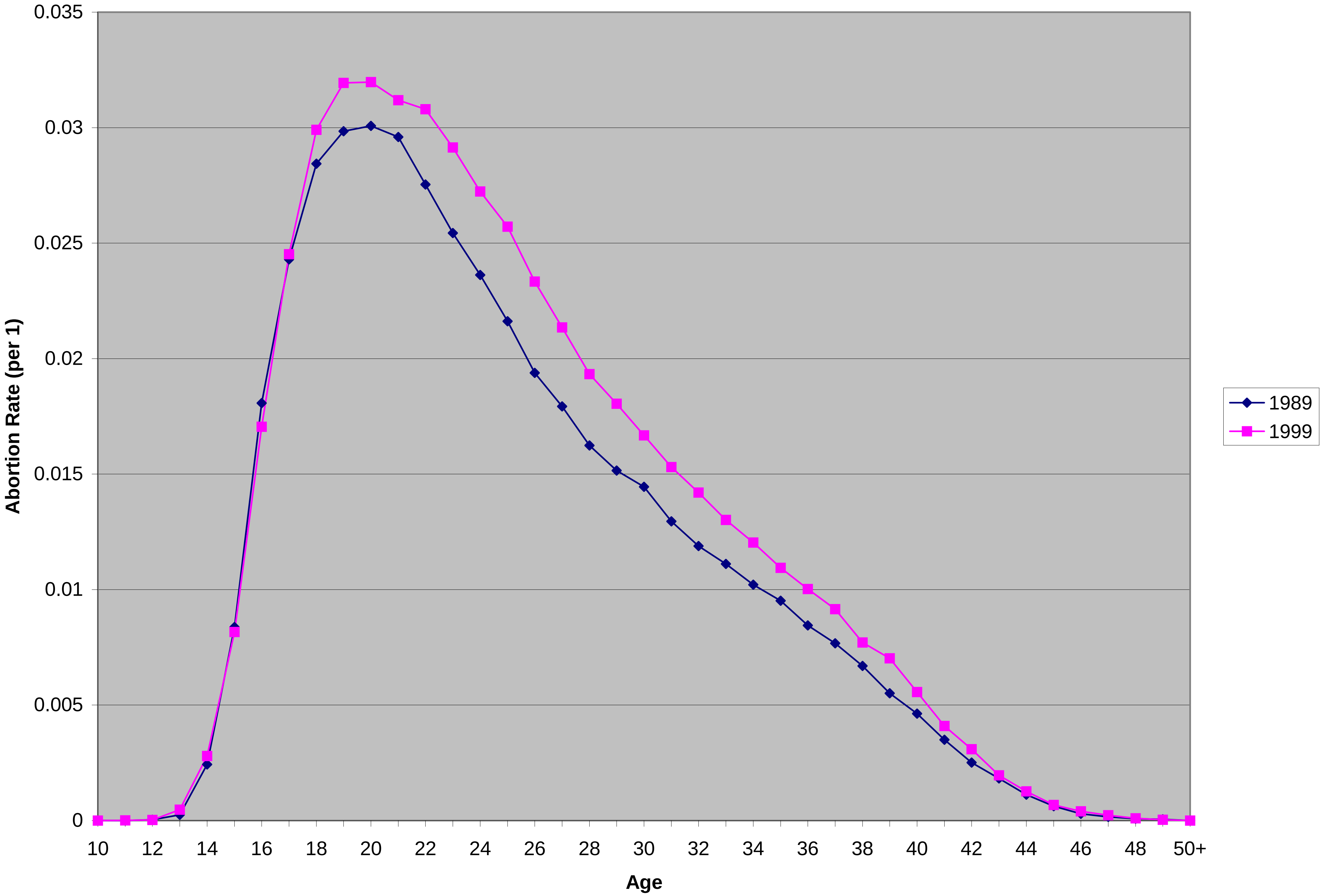

Figure 3
Total Abortion Rates: Scotland vs. England and Wales

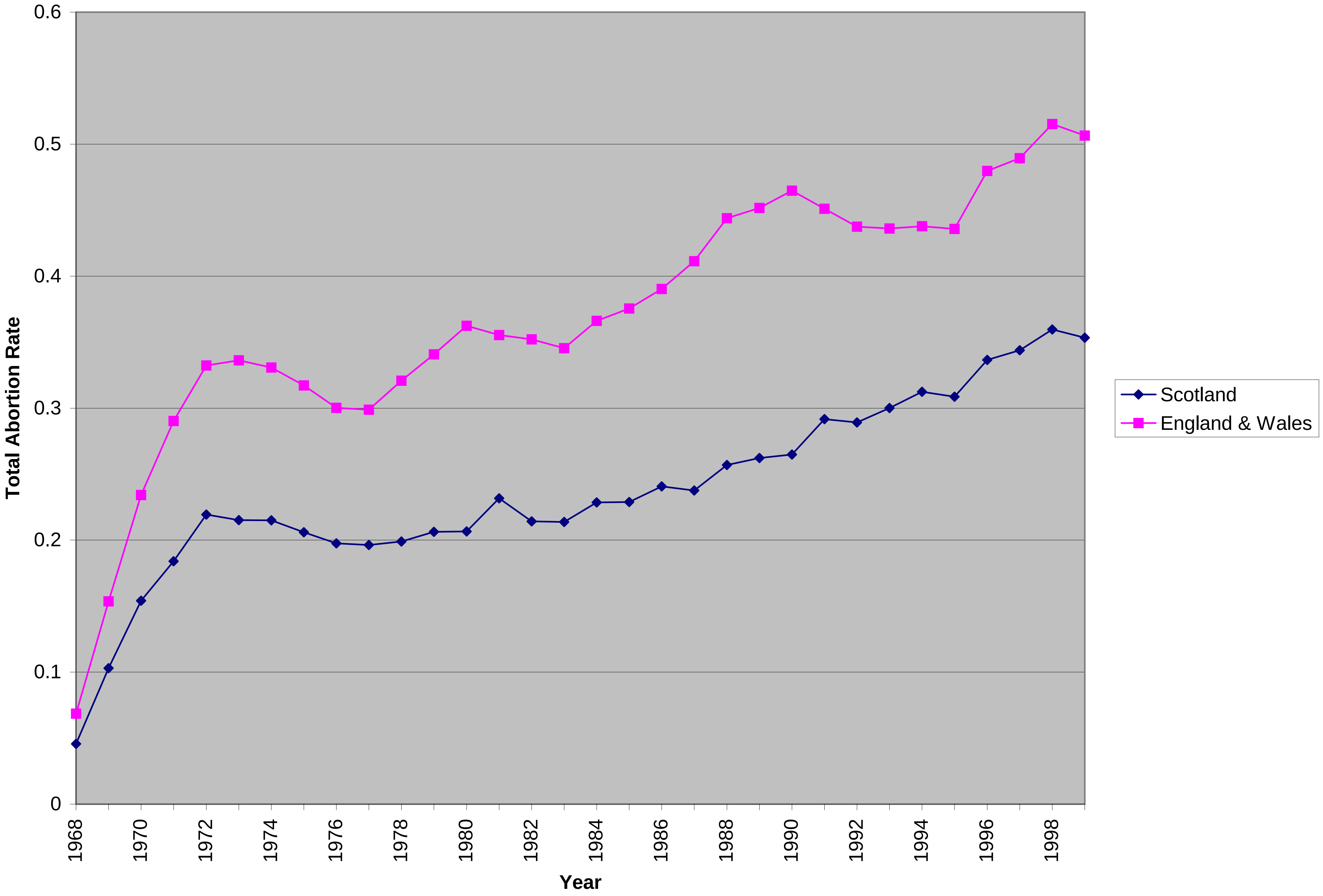

Figure 4
Birth Cohorts: Women in England and Wales
Cumulated Breast Cancer Incidence Within Ages 45-49 vs. Cumulated Abortion Rate

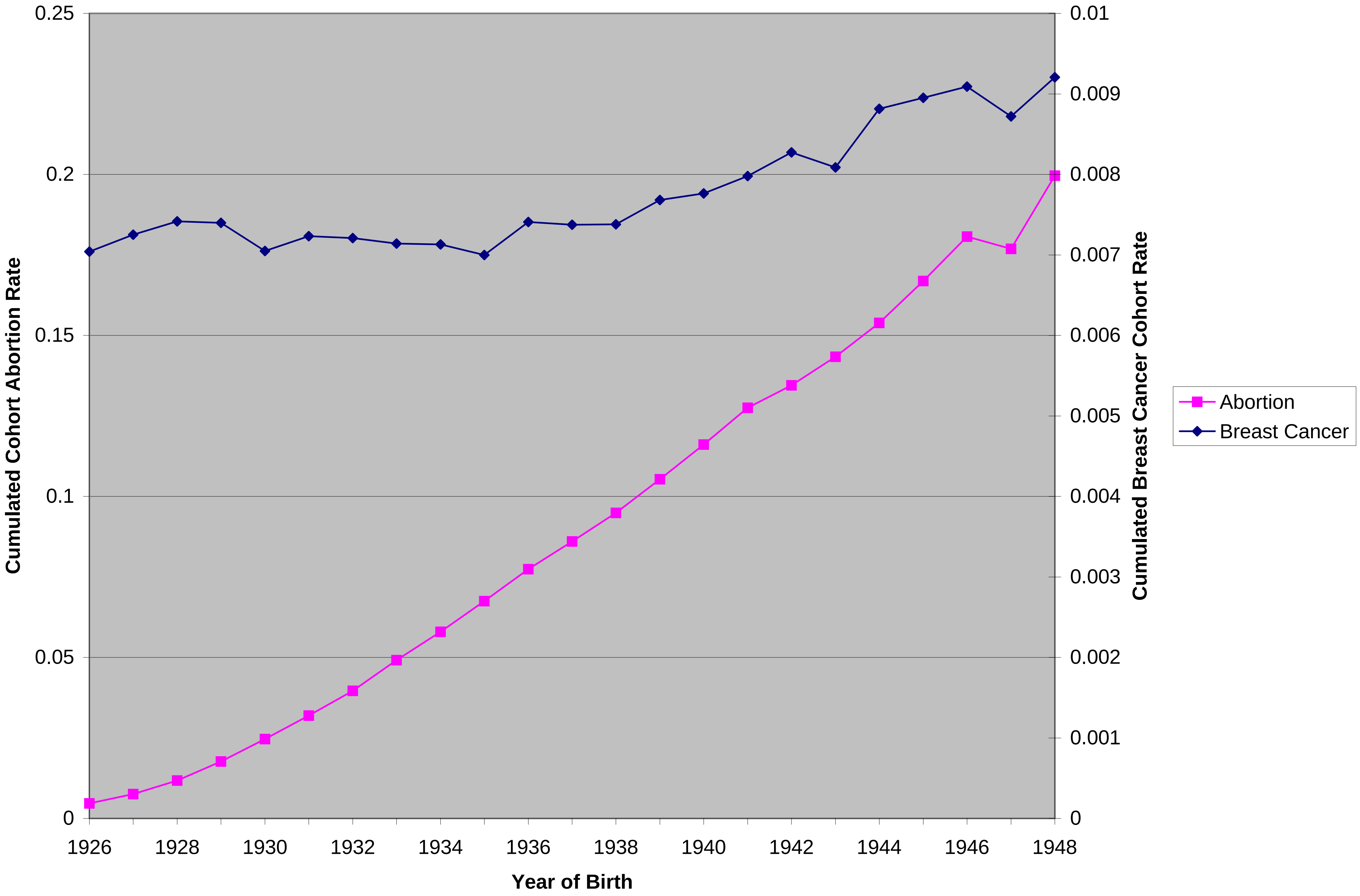

Figure 5
England and Wales: Cohort Mean Age at First Birth vs. Cumulated Cohort Breast Cancer Within Ages 45-49

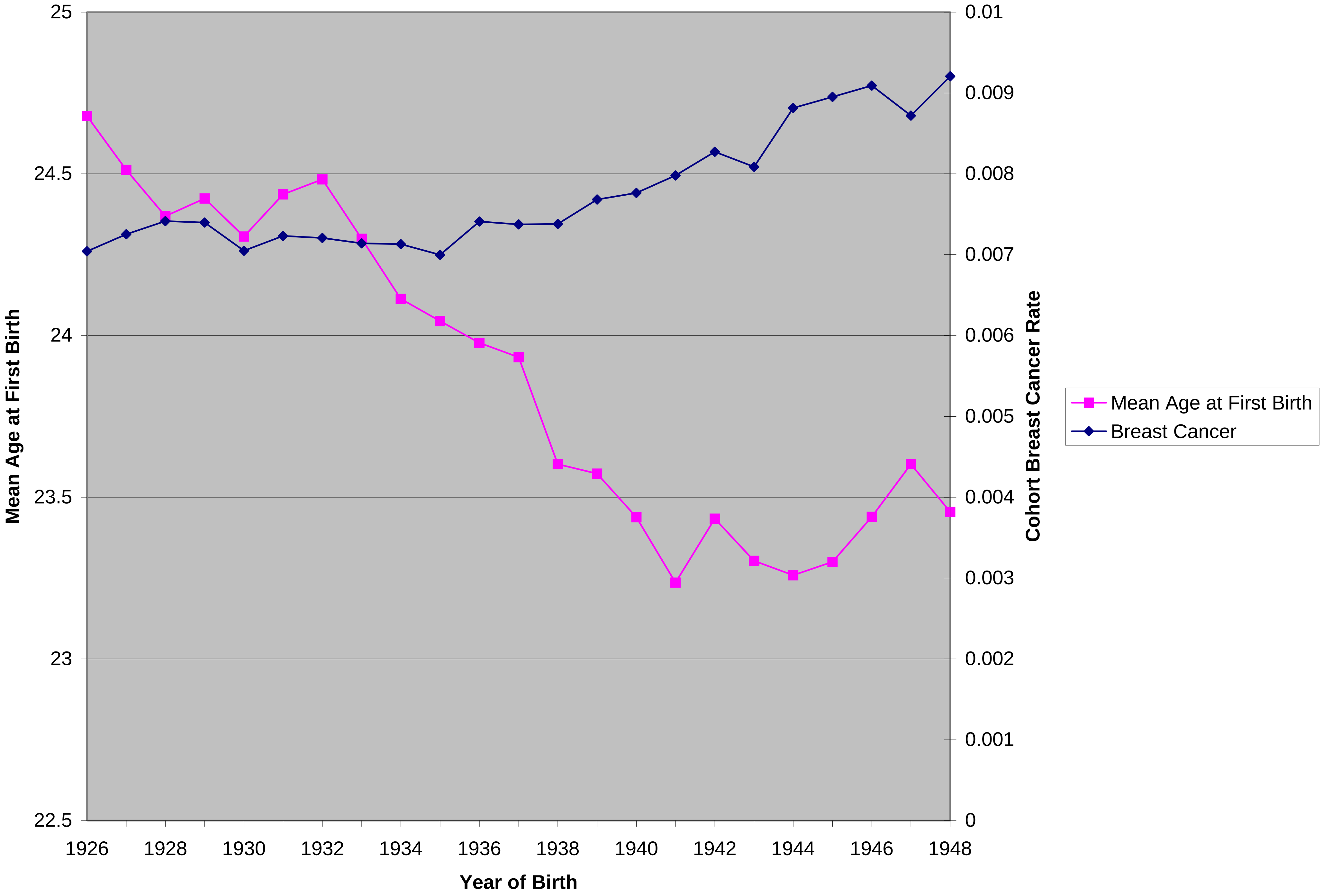

Figure 6
England and Wales: Cumulated Cohort Breast Cancer Rates Within Ages 45-49 vs. Cohort Childlessness

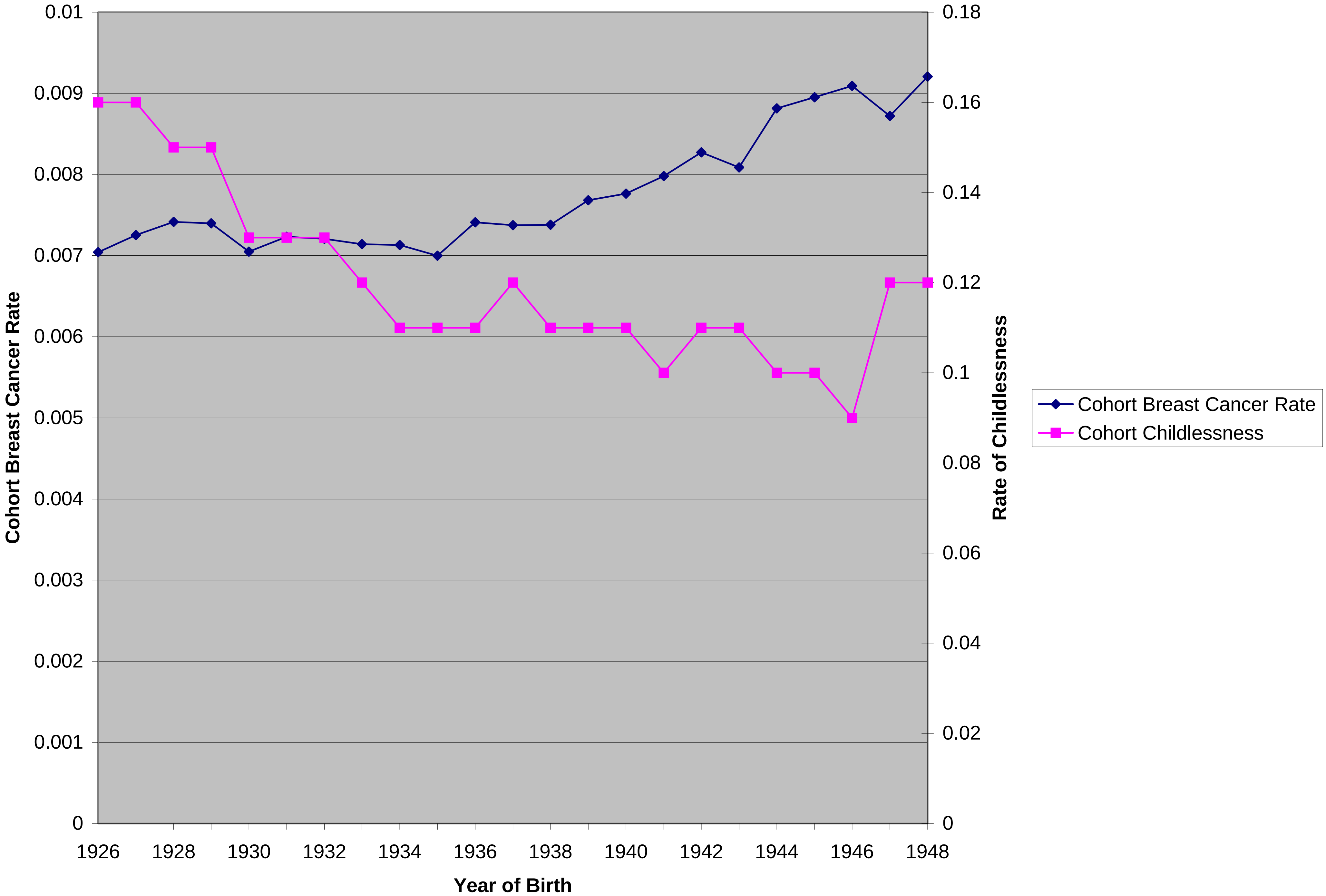

Figure 7
Birth Cohorts: Women in England and Wales
Cumulated Breast Cancer Incidence within Ages 45-49 vs. Average Number of Children

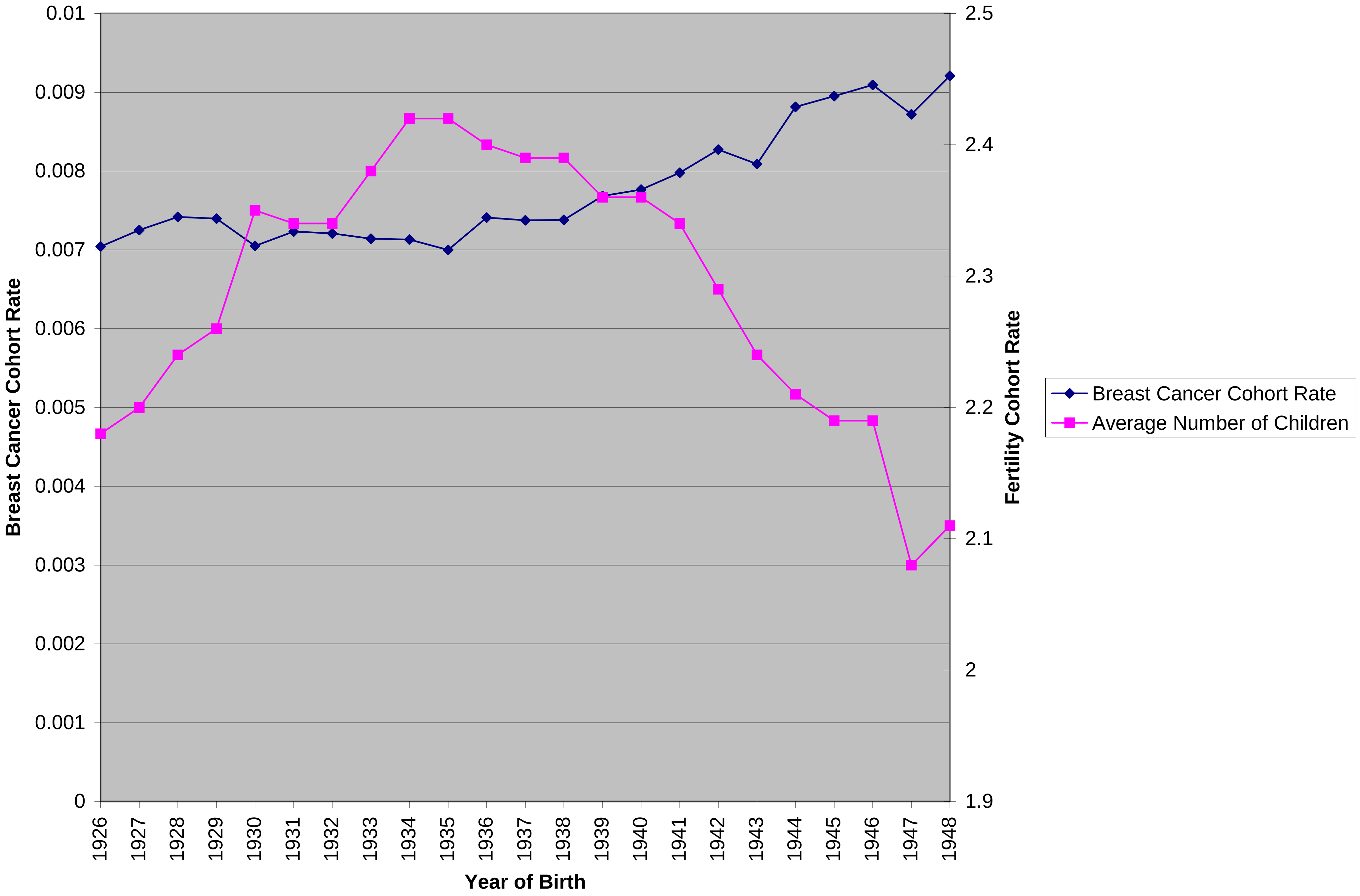

Figure 8
England and Wales. Parous vs. Nulliparous Abortion Rates 1968-1999

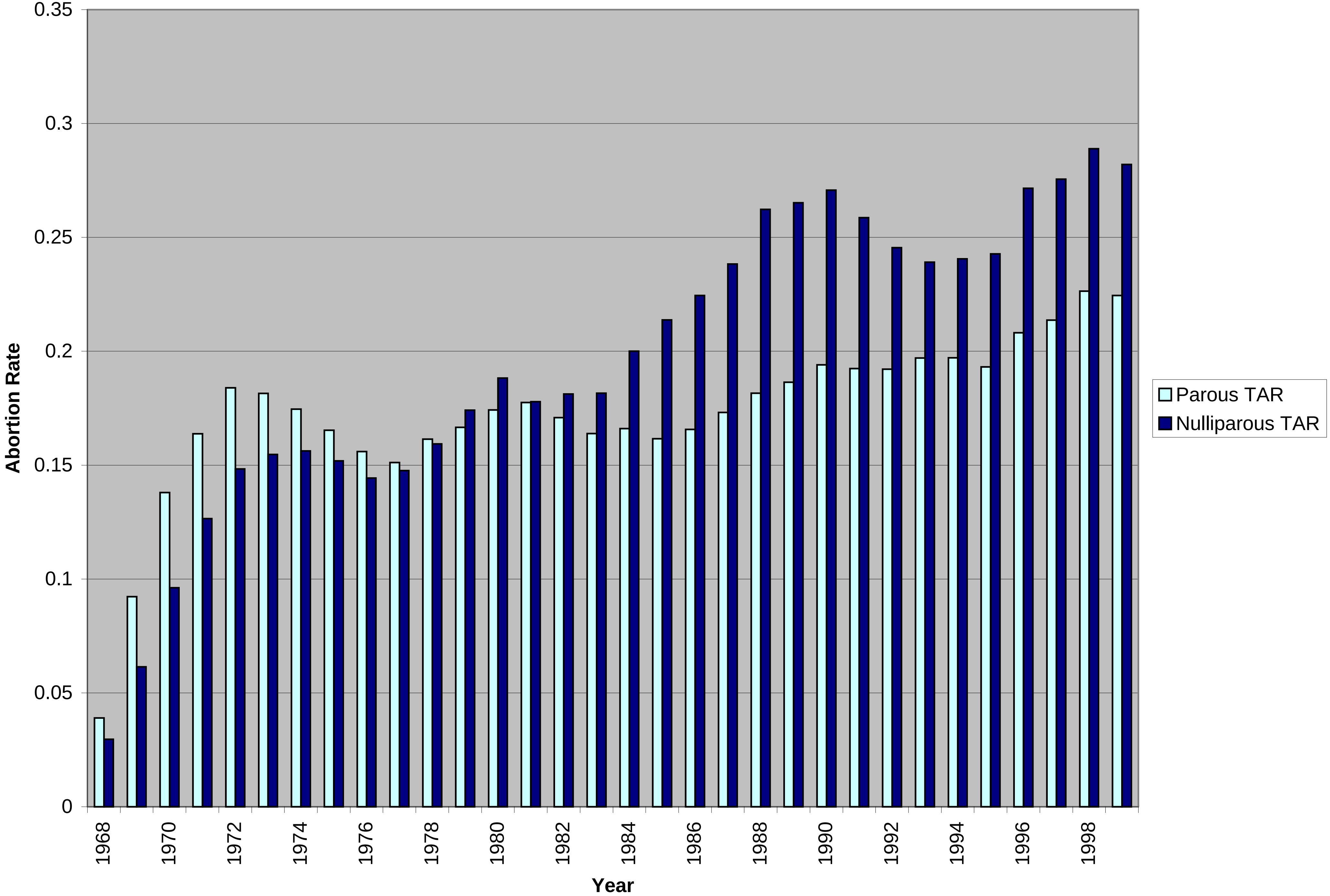

Figure 9
Women in England and Wales: Cumulated Cohort Rates of Abortion (Parous and Nulliparous) vs. Cumulated Cohort Rate of Breast Cancer for Women Within Ages 45-49

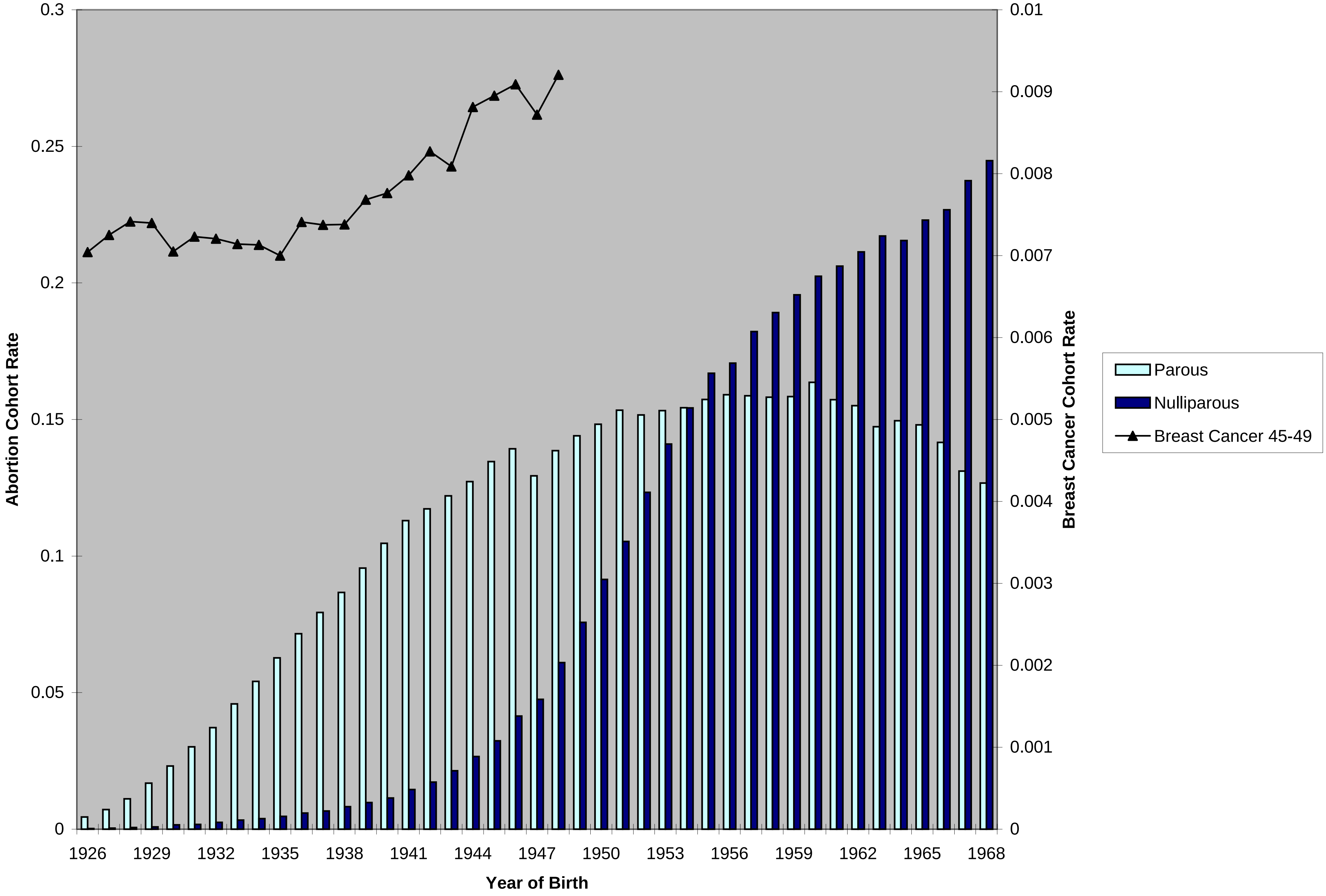

Figure 10
Birth Cohorts: Women in Scotland
Cumulated Breast Cancer Incidence Within Ages 45-49 vs. Cumulated Abortion Rate

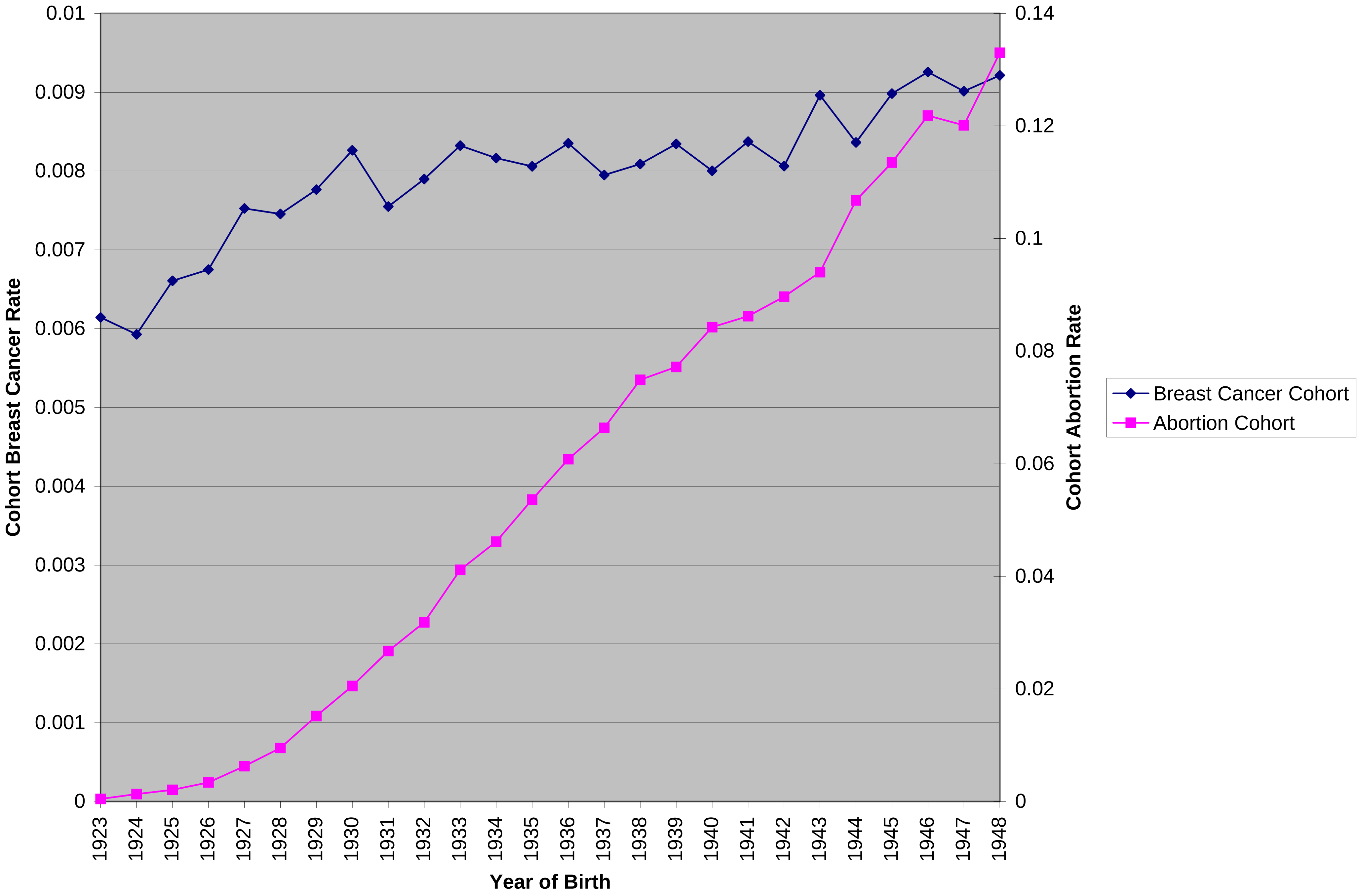

Figure 11
Birth Cohorts: Women in Scotland
Cumulated Breast Cancer Incidence Within Ages 45-49 vs. Cohort Fertility

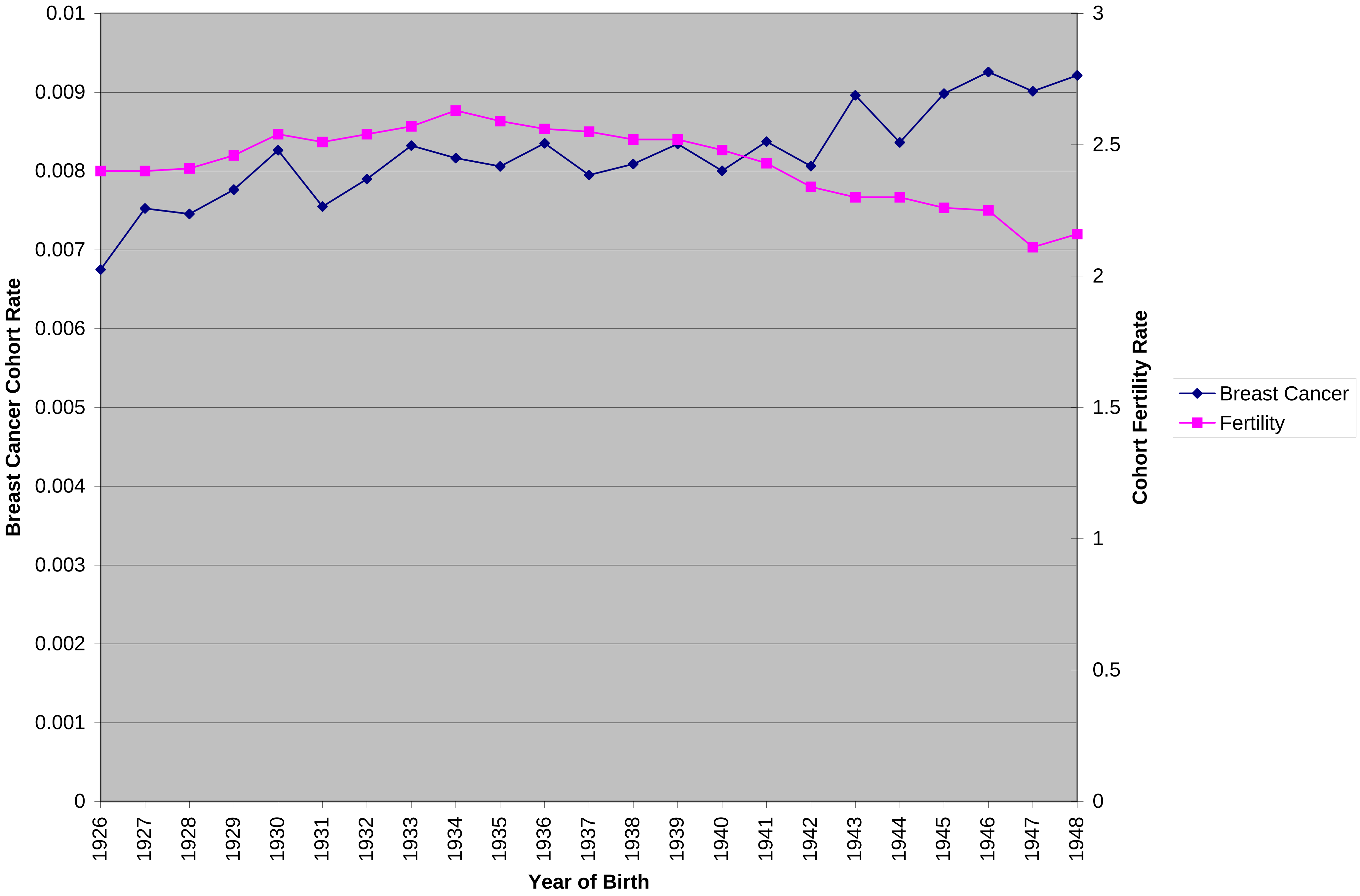

Figure 12
Average Yearly Rates of Incidence of Malignant Female Breast Cancer in Scotland within Age Groups 40-44, 45-49 and 50-54 from 1960-1997

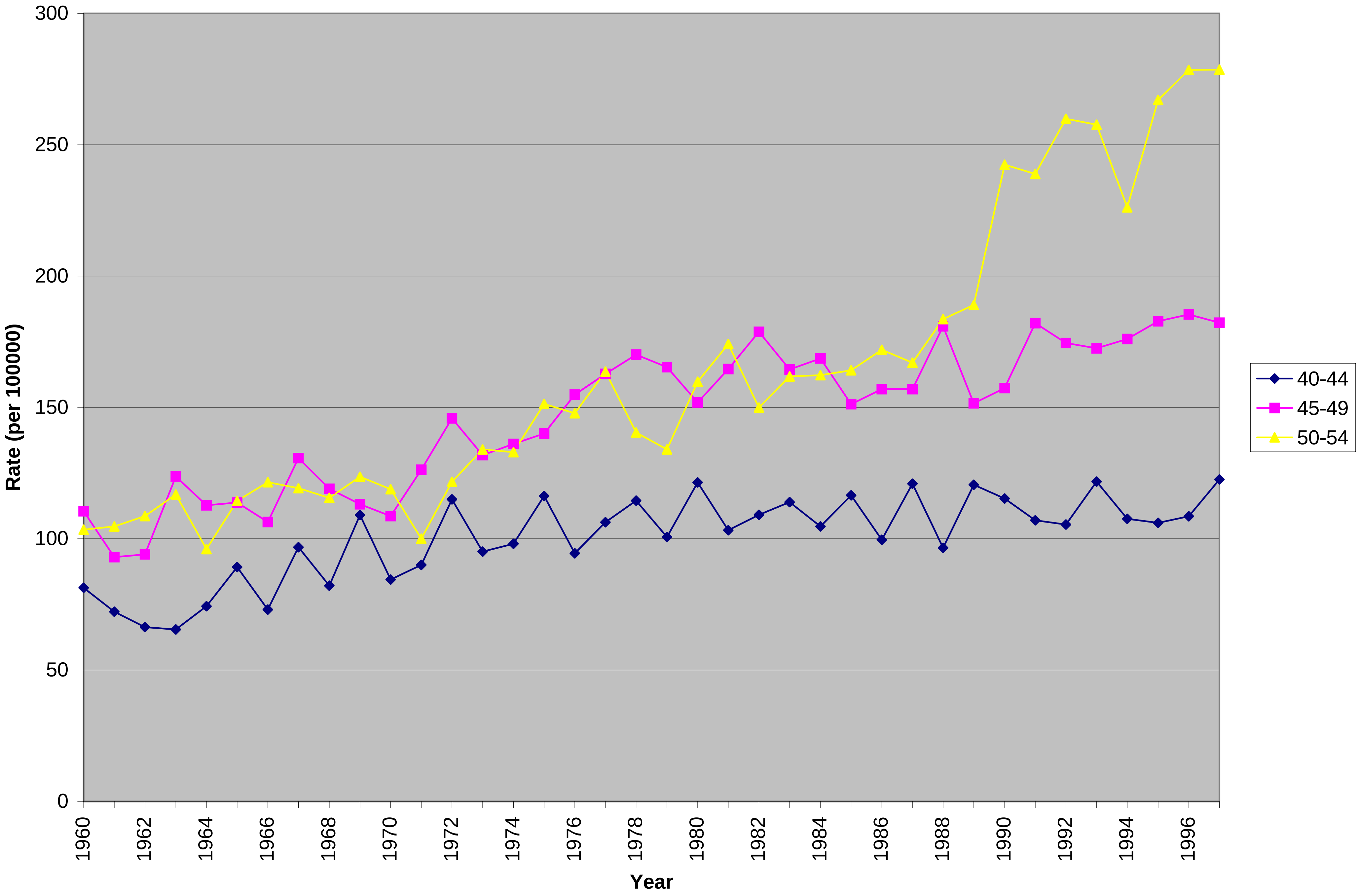

Figure 13
Women in Scotland: Parous vs. Nulliparous Abortion Rates 1968-2000

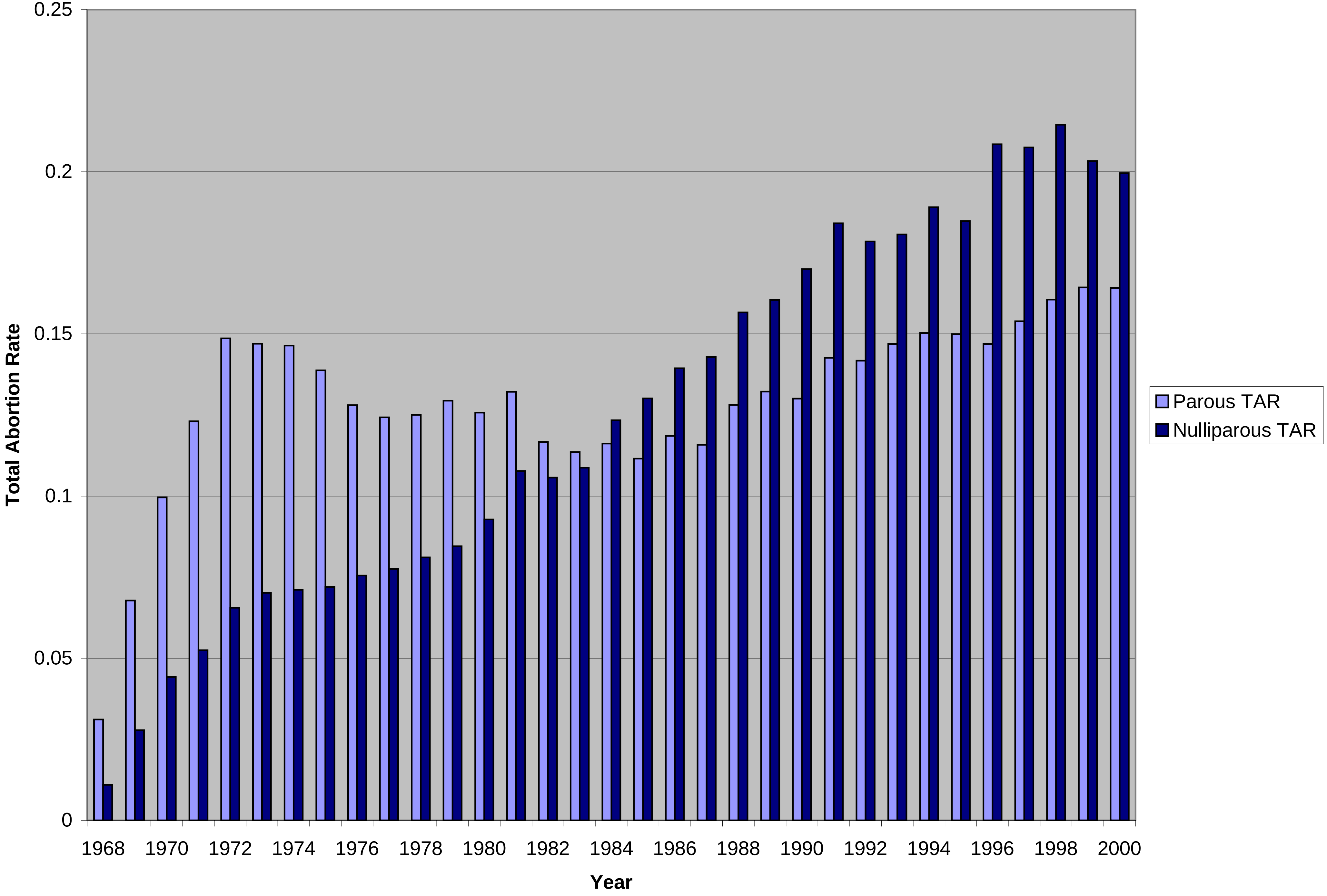

Figure 14

Scotland - Cumulated Cohort Parous and Nulliparous Abortion Rates vs. Cumulated Cohort Breast Cancer Rates Within Ages 45-49

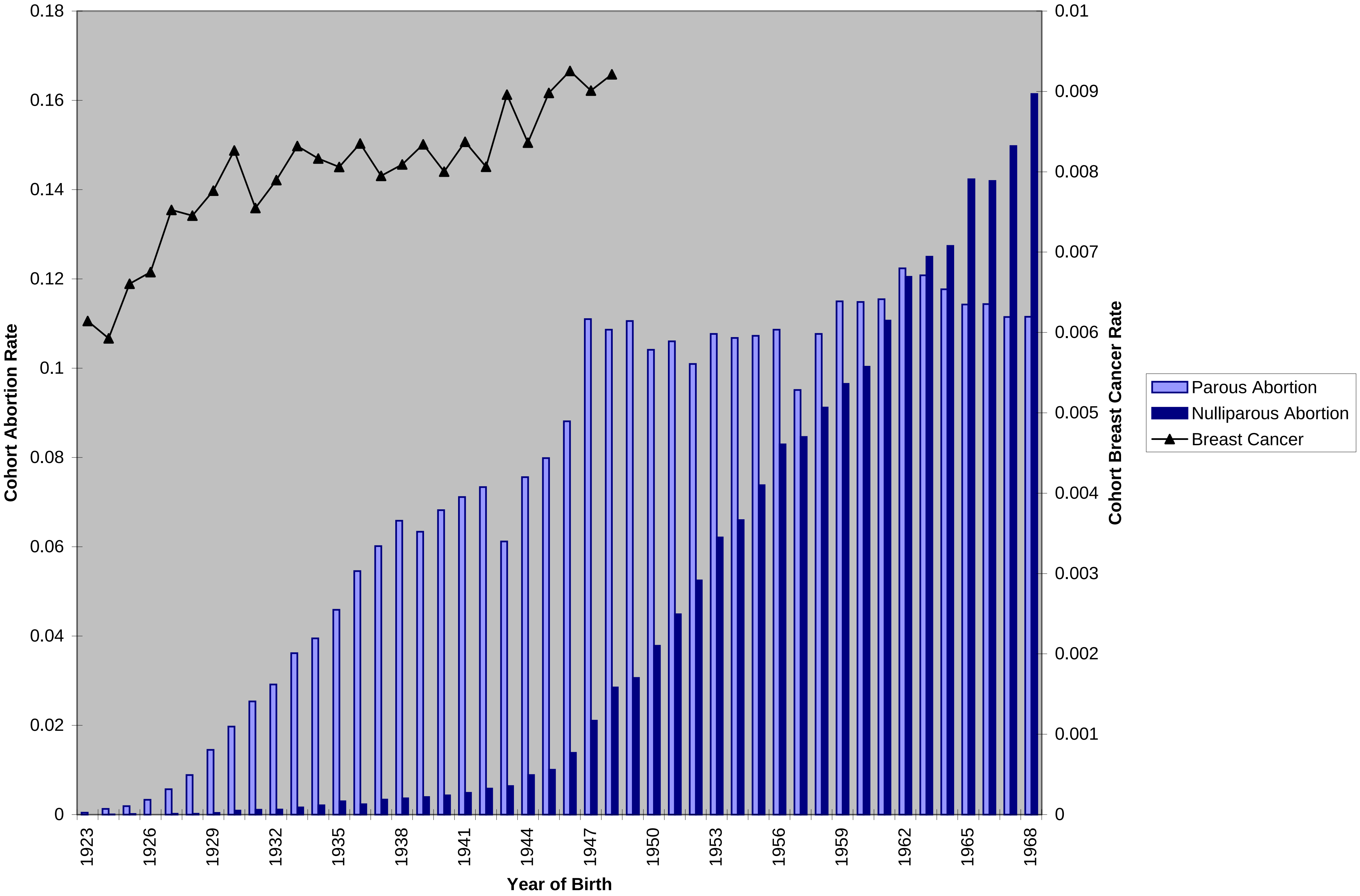

Figure 15
Scotland vs. Sweden - Breast Cancer Incidence Rates Within Ages 45-49

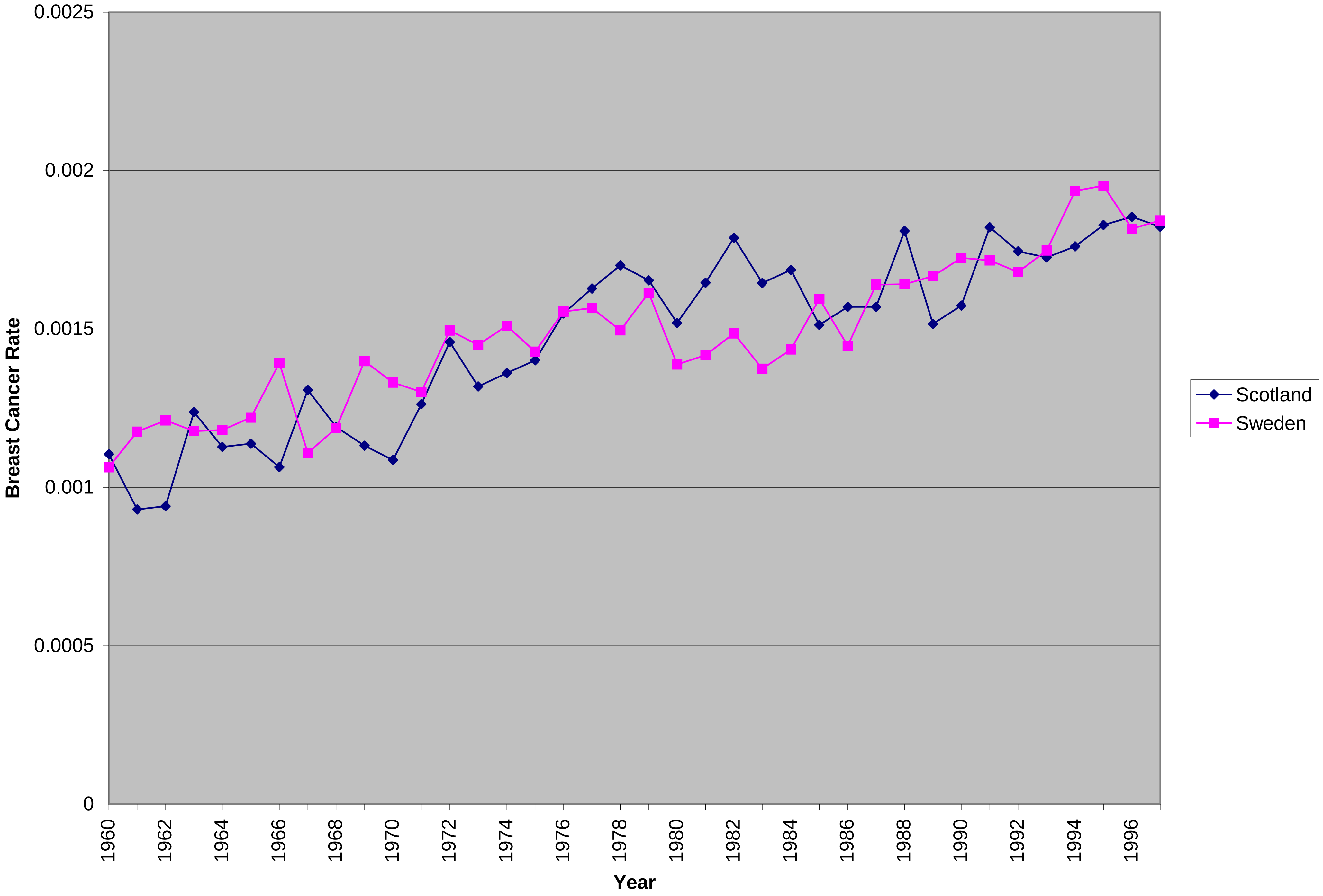

Figure 16

Scotland vs. Sweden - Breast Cancer Incidence Rates Within Ages 50-54

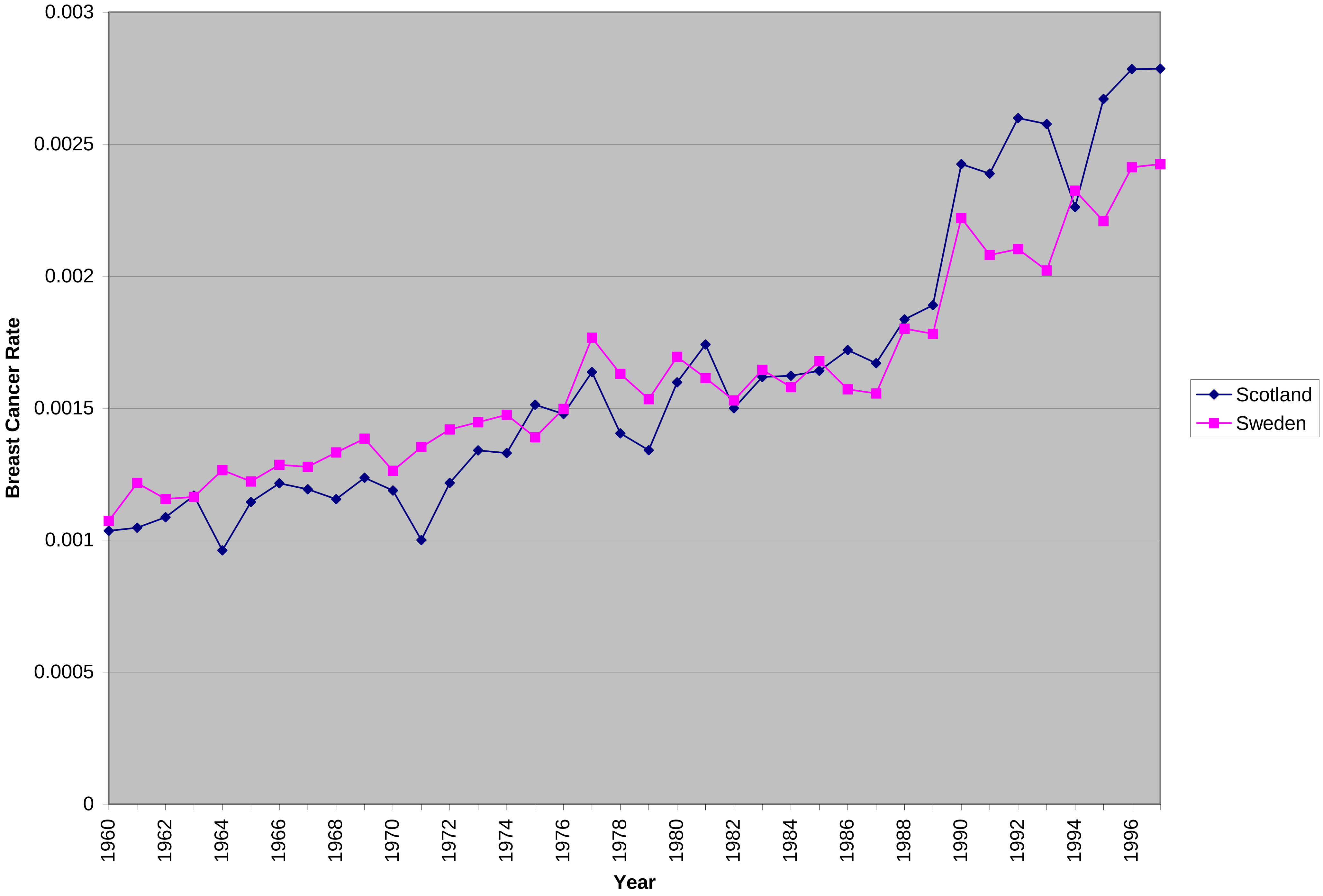

Figure 17
Total Abortion Rates Compared: Sweden, England and Wales and Scotland. 1975-1999

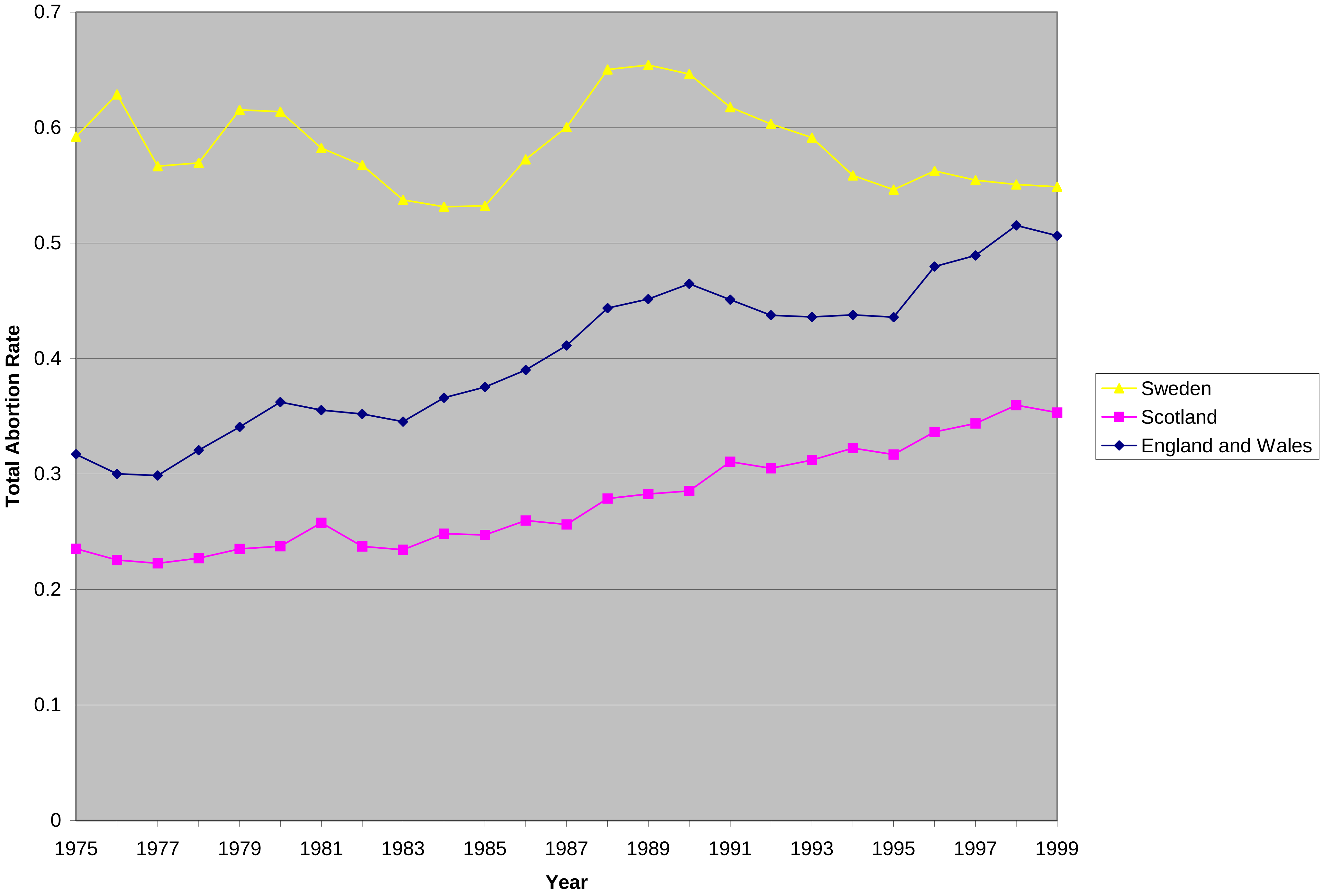

Figure 18
Comparison of Age Specific Abortion Rates for 1999: Sweden vs. England and Wales

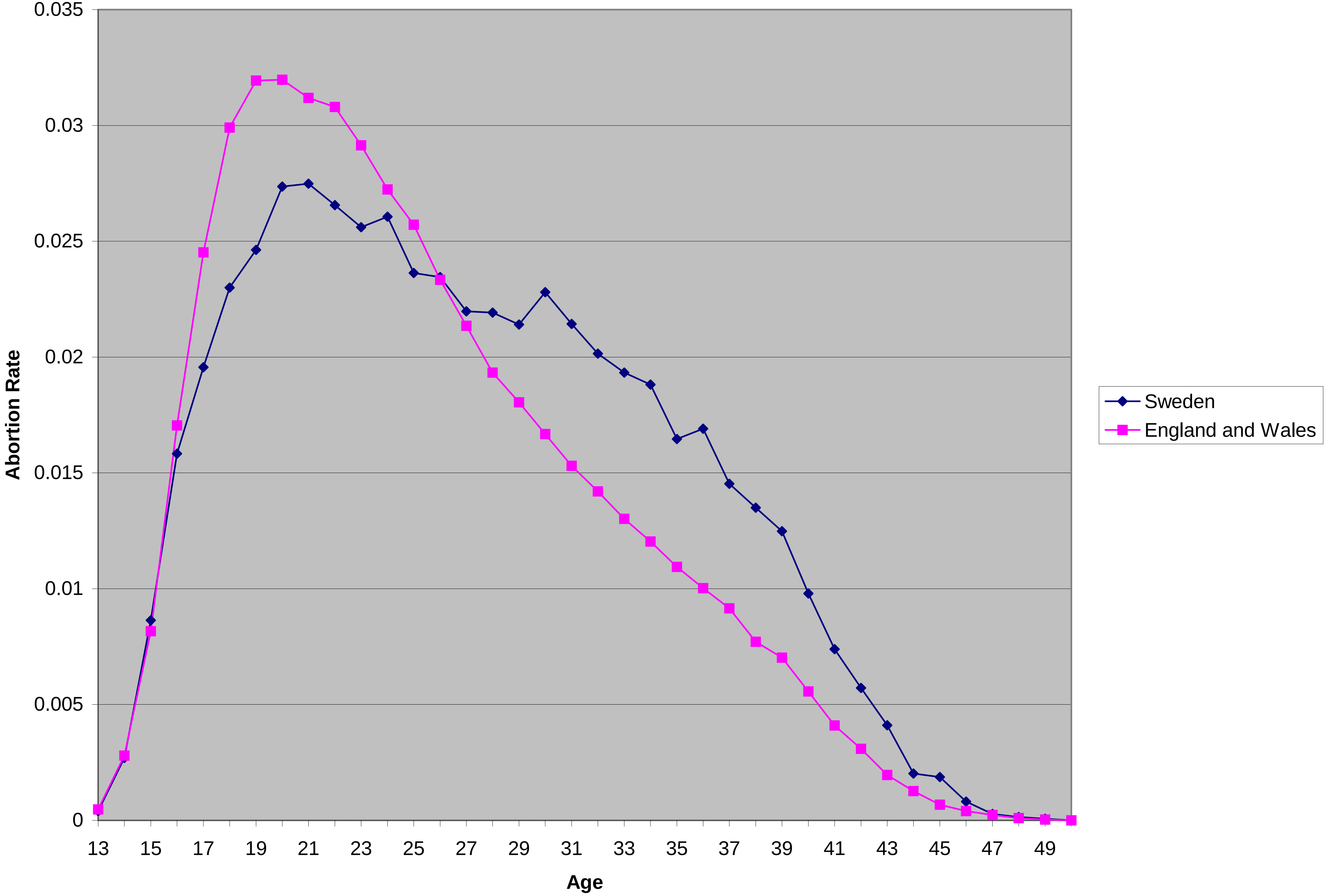

Figure 19

Sweden - Cumulated Cohort Breast Cancer Rates Within Ages 45-49 vs. Cumulated Cohort Abortion Rate (Abortions Since 1975)

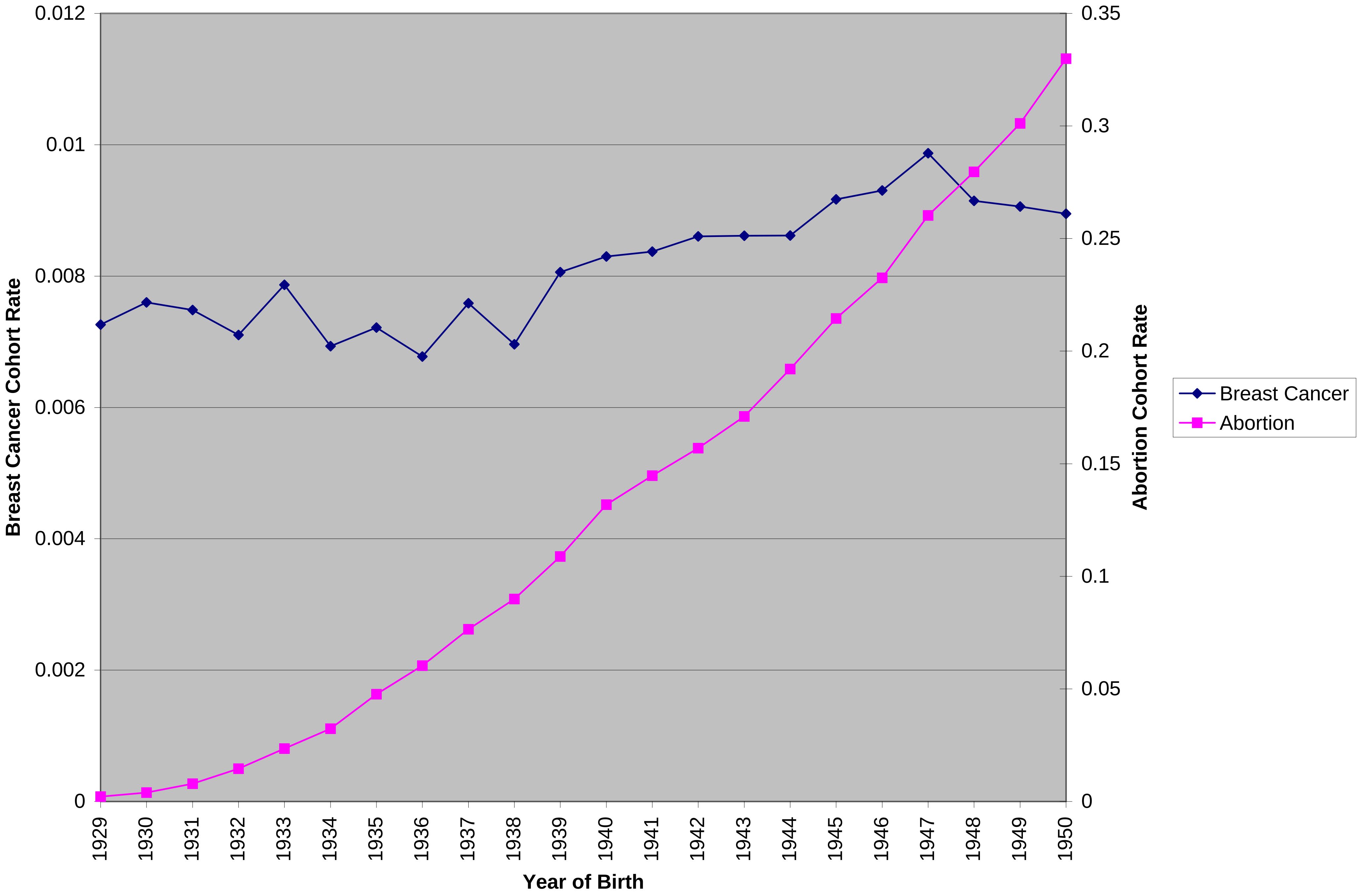

Figure 20
Sweden - Cumulated Cohort Breast Cancer Rates Within Ages 45-49 vs. Cohort Fertility Rate

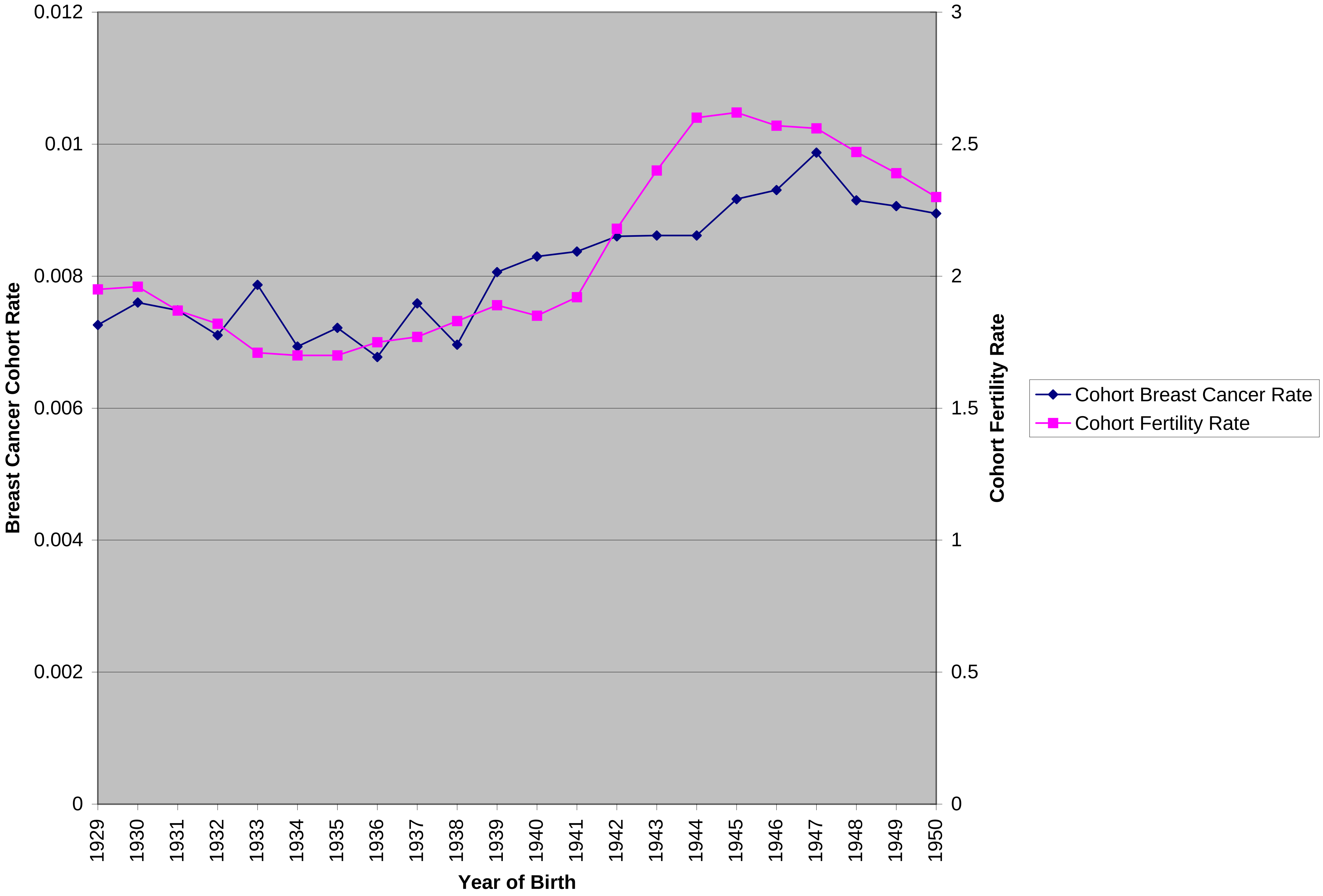

Figure 21
Sweden - Trend of Parous vs. Nulliparous Total Abortion Rates. 1975-2000

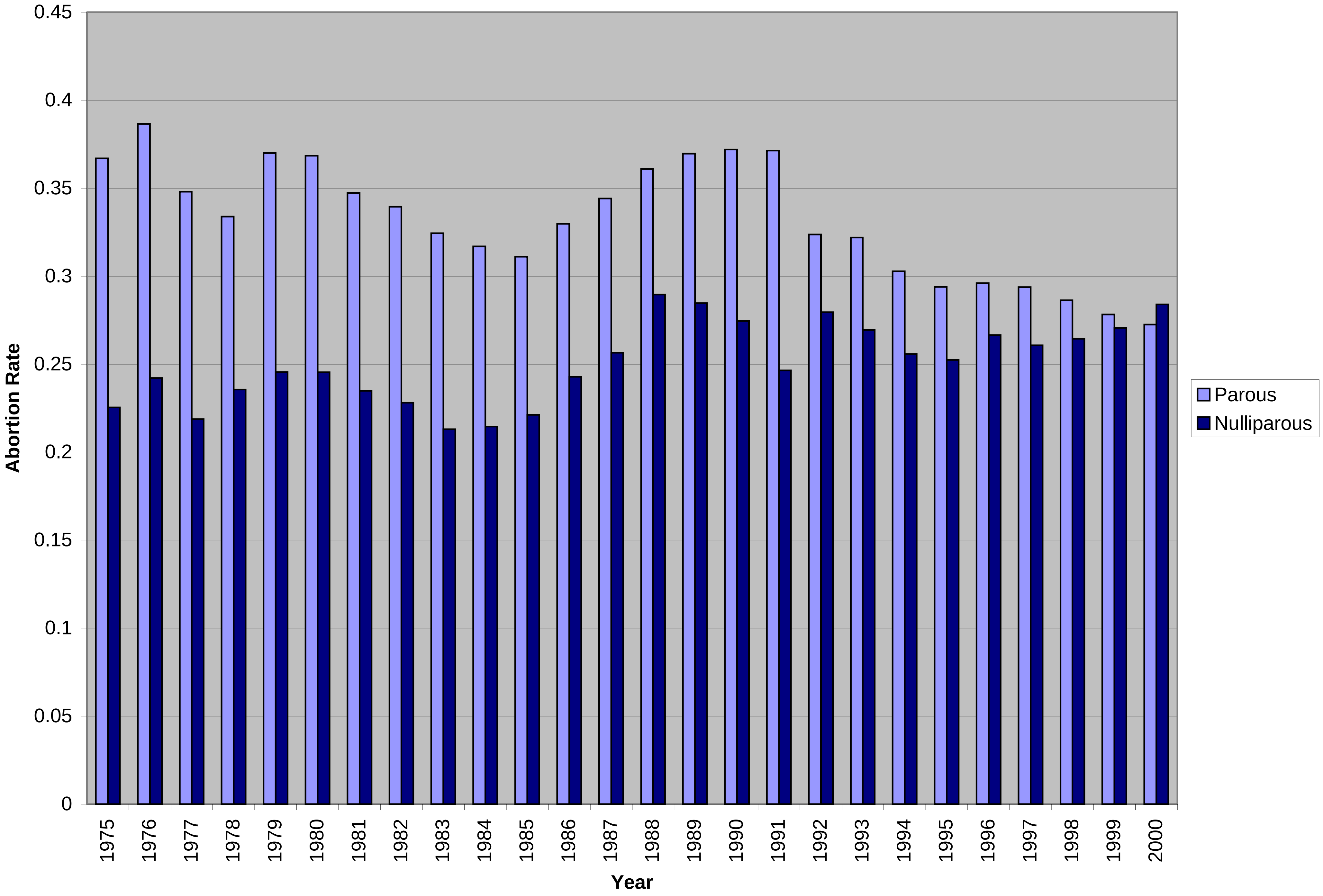

Figure 22
Sweden - Cumulated Cohort Breast Cancer Rates over Ages 45-49 vs. Cumulated Cohort Nulliparous and Parous Abortion Rates

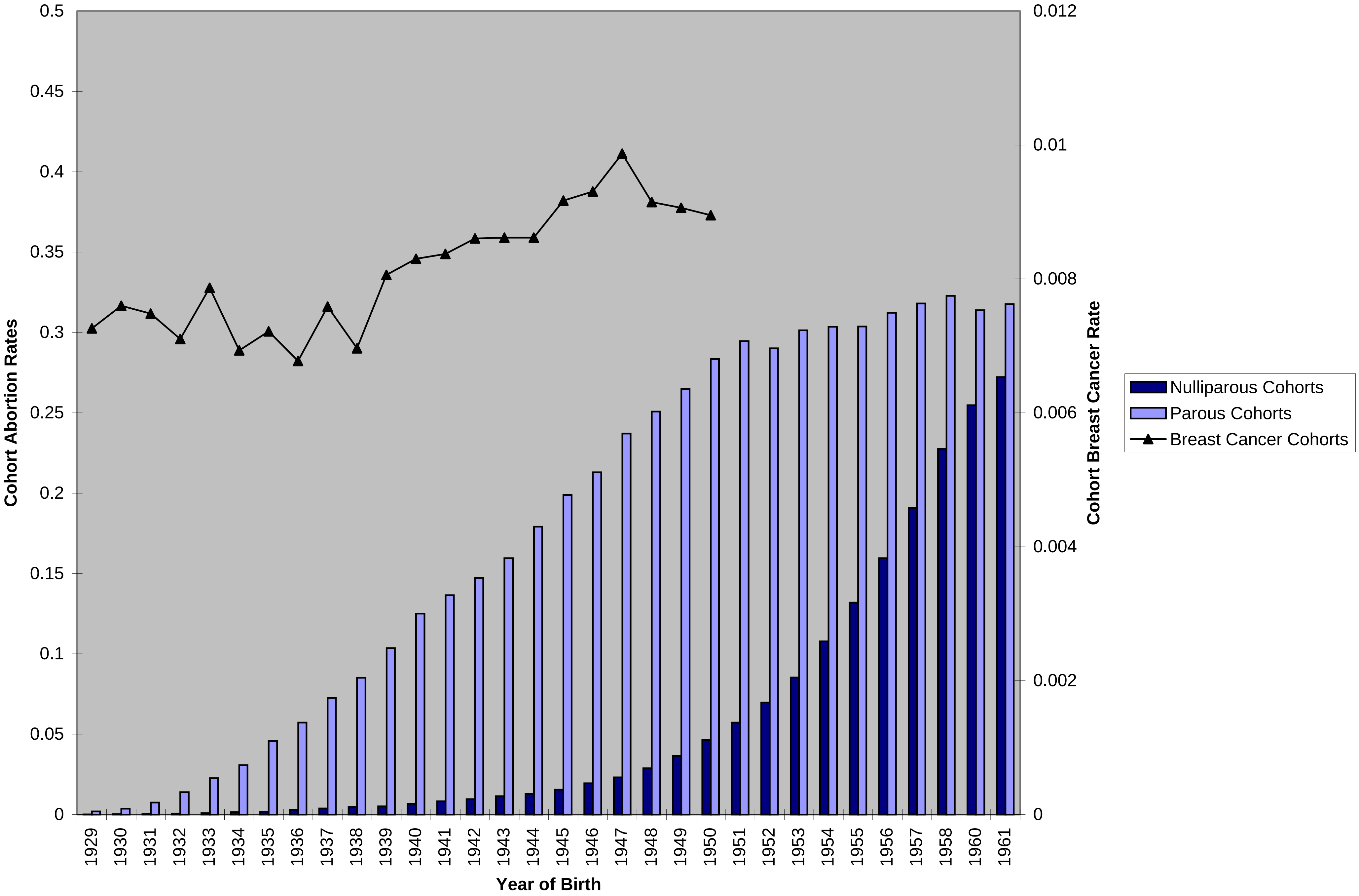

Figure 23
Average Yearly Rates of Incidence of Malignant Female Breast Cancer in Finland within Age Groups 40-44, 45-49 and 50-54 from 1975-1997

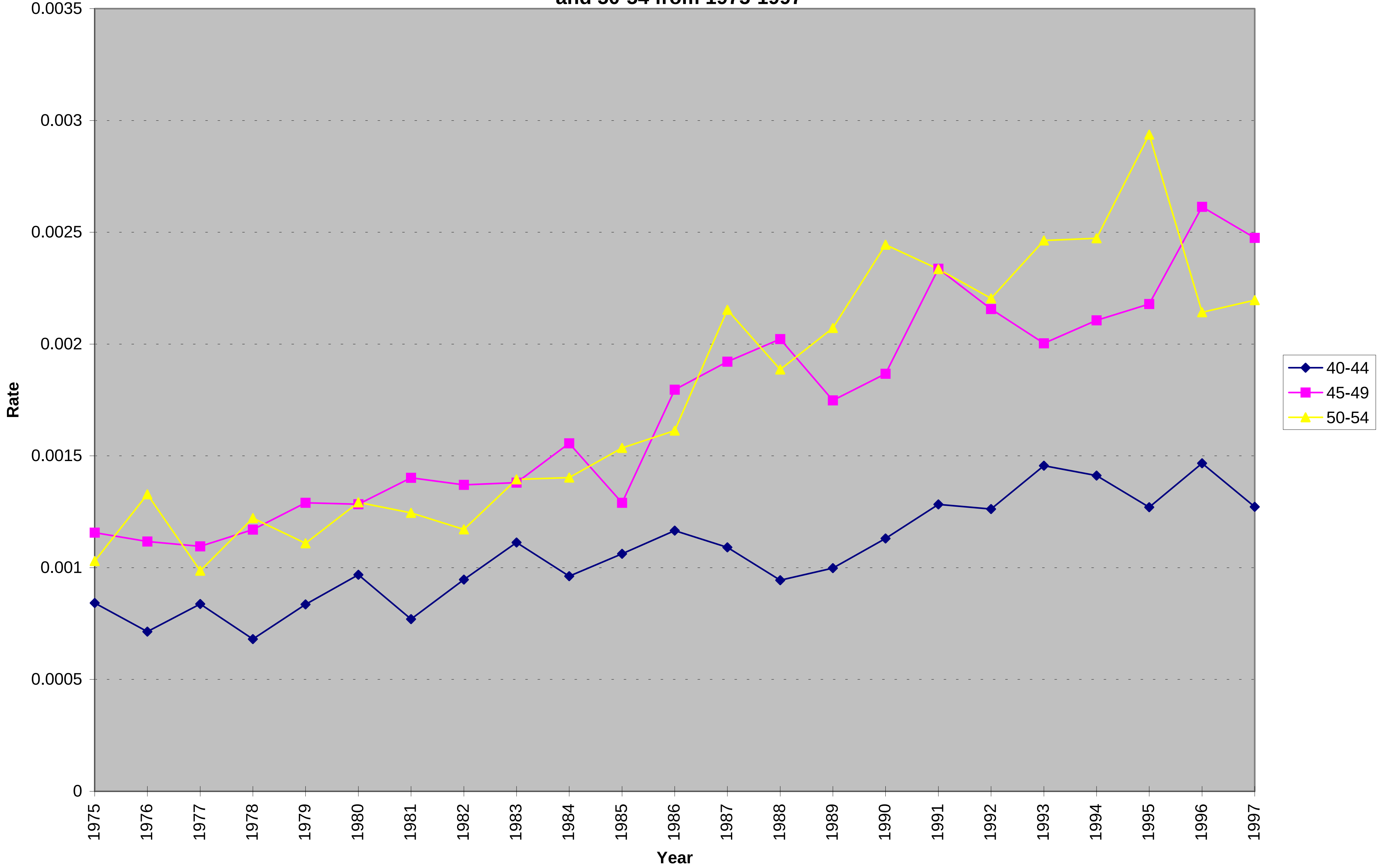

Figure 24
Abortion Rates By Age Group: FINLAND 1975-1997

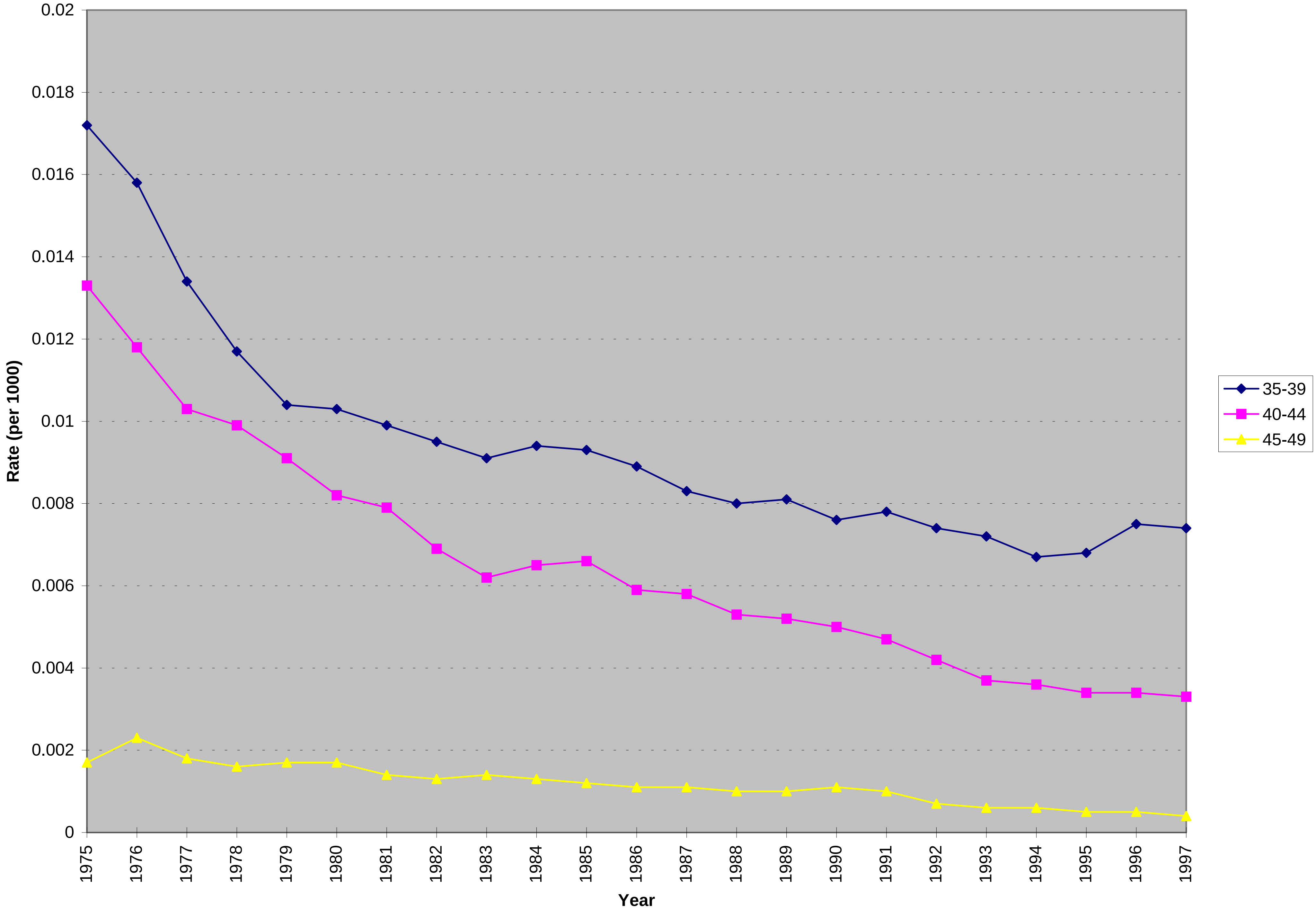

Figure 25
The Czech Republic - Breast Cancer Trends Within Ages 40-44,45-49 and 50-54 from 1977-1996

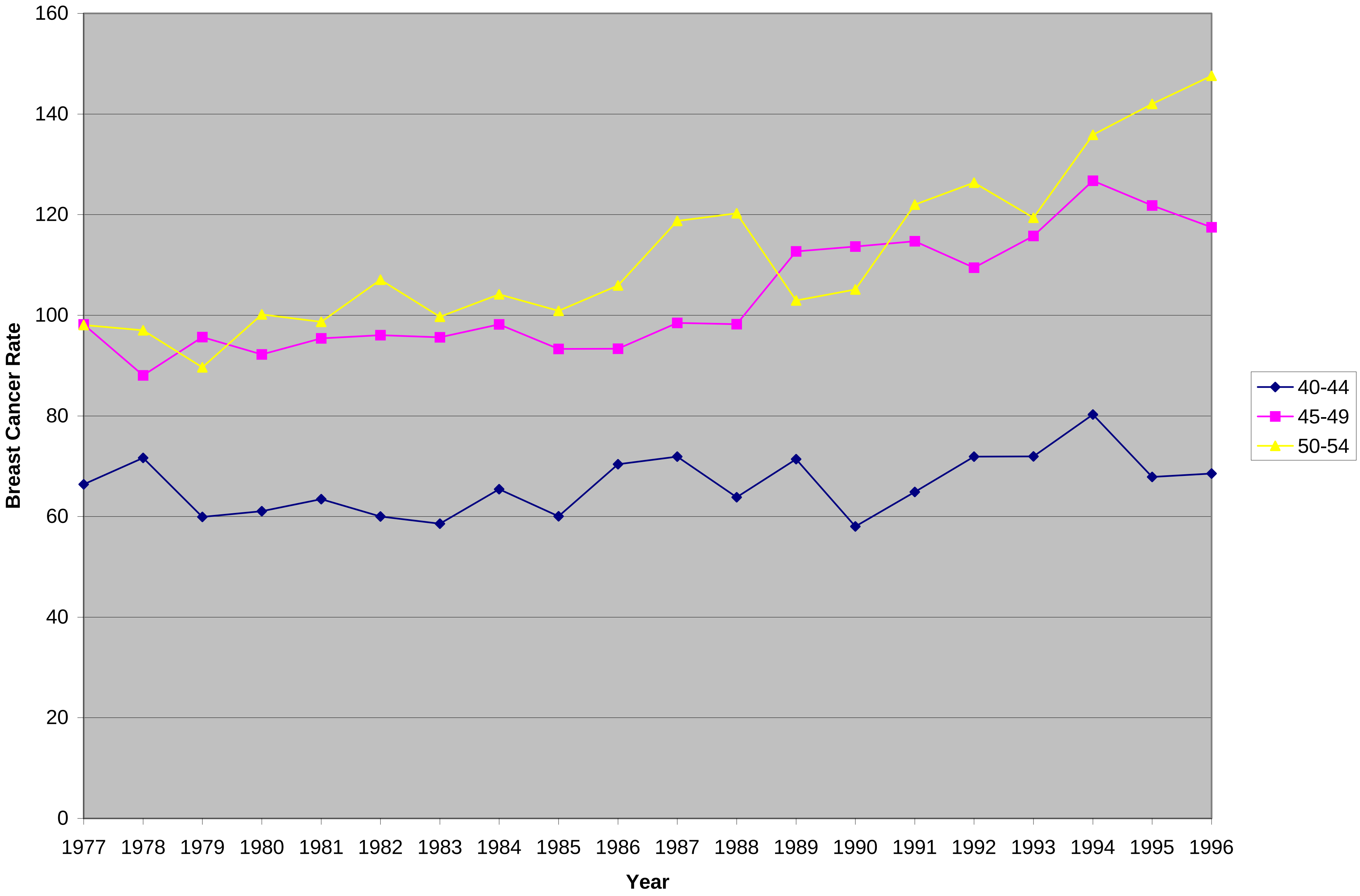

Figure 26
Trends in Total Abortion Rates - The Czech Republic vs. England and Wales. 1968-1997

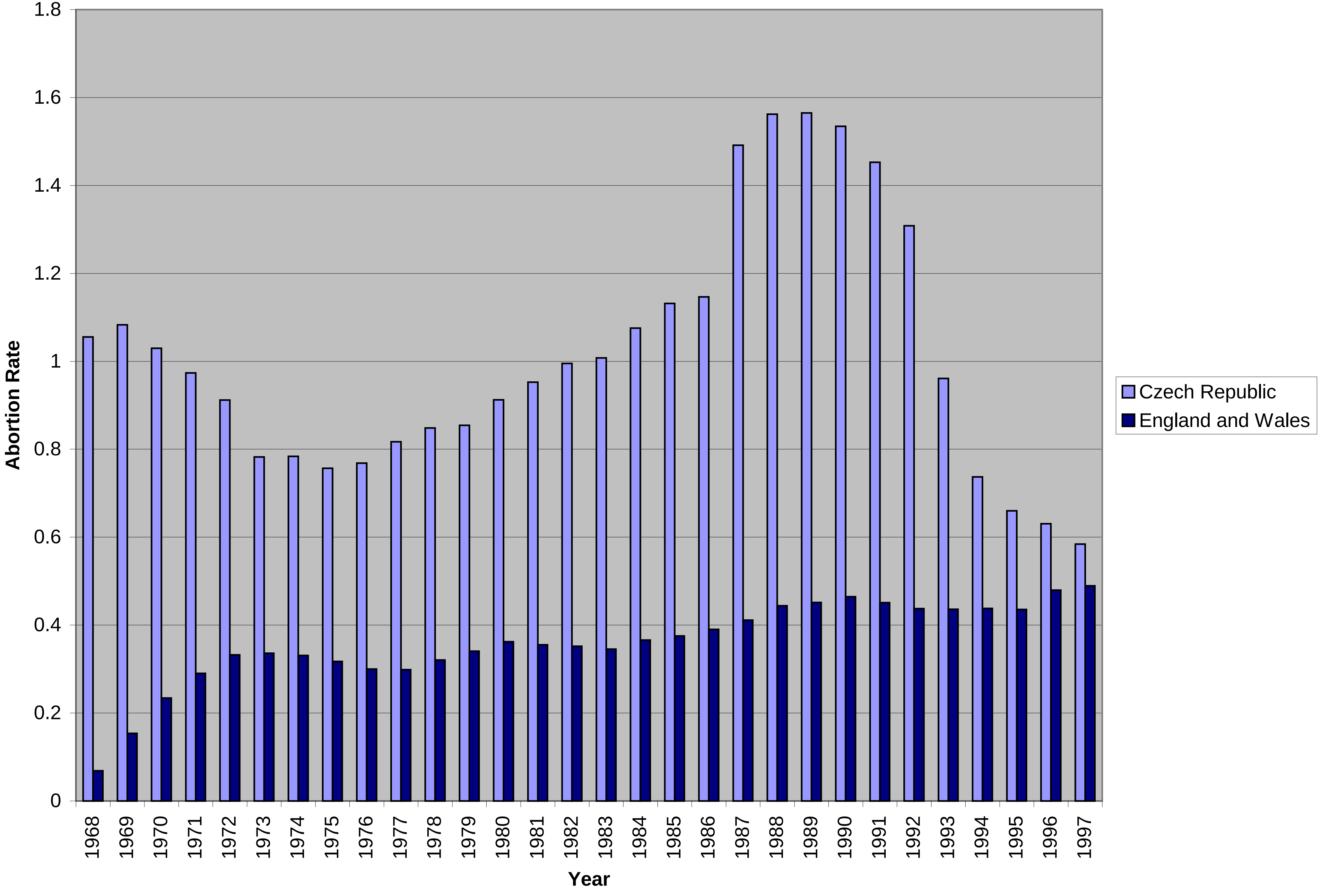

Figure 27
The Czech Republic vs. England and Wales.
Comparison of Age Specific Abortion Rates for 1997.

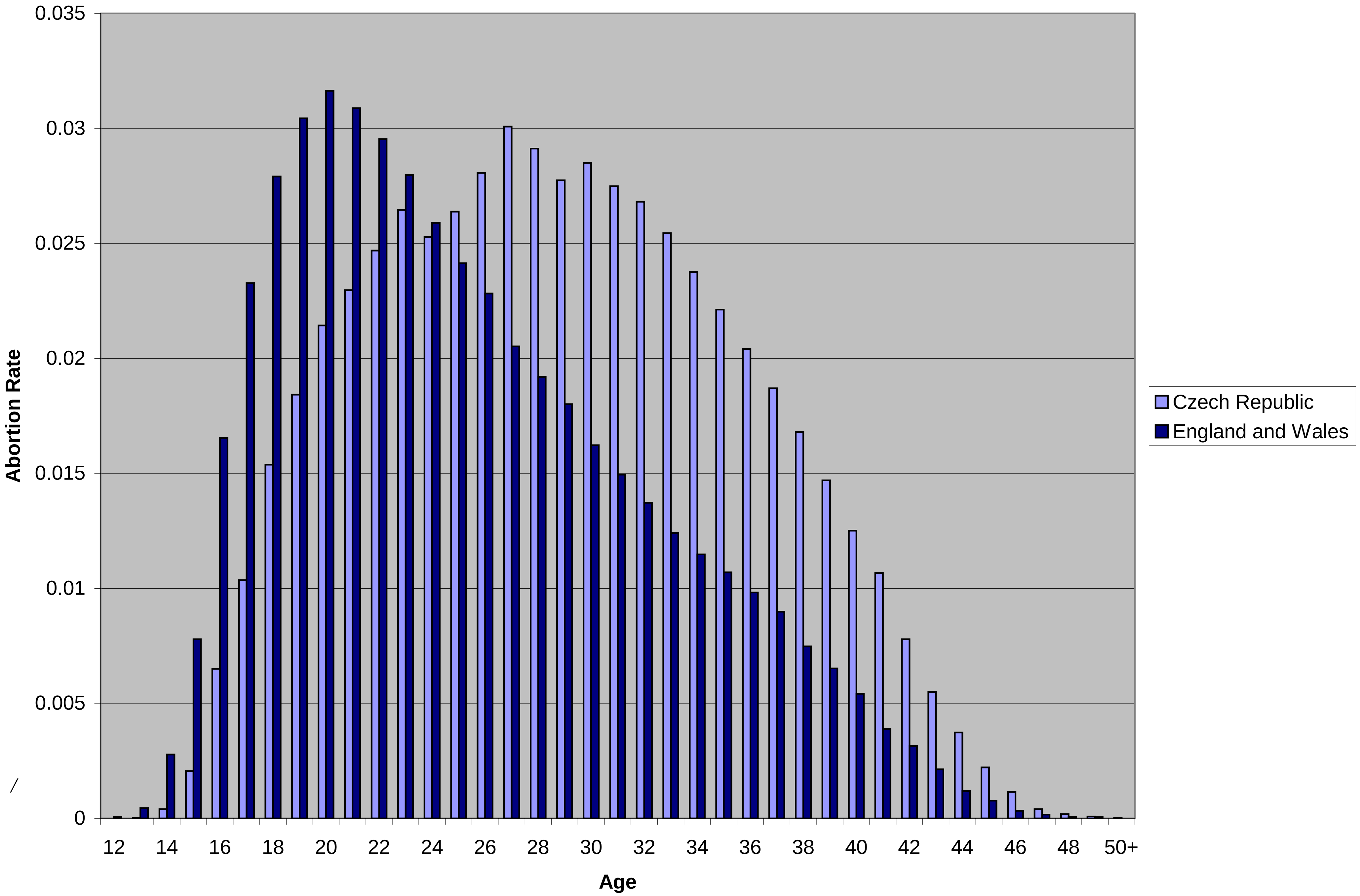

Figure 28
The Czech Republic. Cumulated Cohort Breast Cancer Rates Within Ages 45-49 vs. Cumulated Cohort Abortion Rates

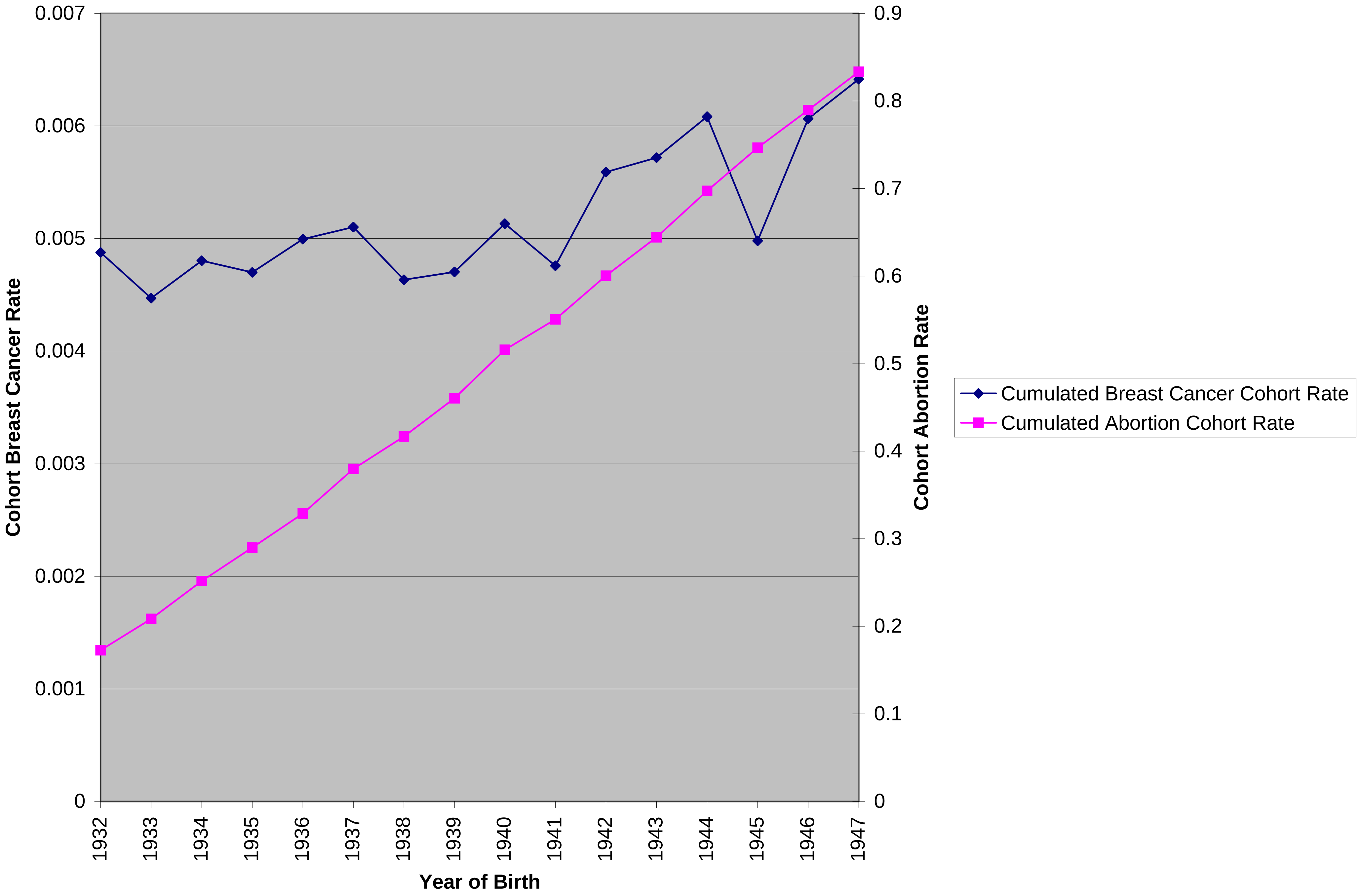

Figure 29
The Czech Republic. Cumulated Cohort Breast Cancer Rates Within Ages 45-49 vs. Cumulated Cohort Fertility Rate

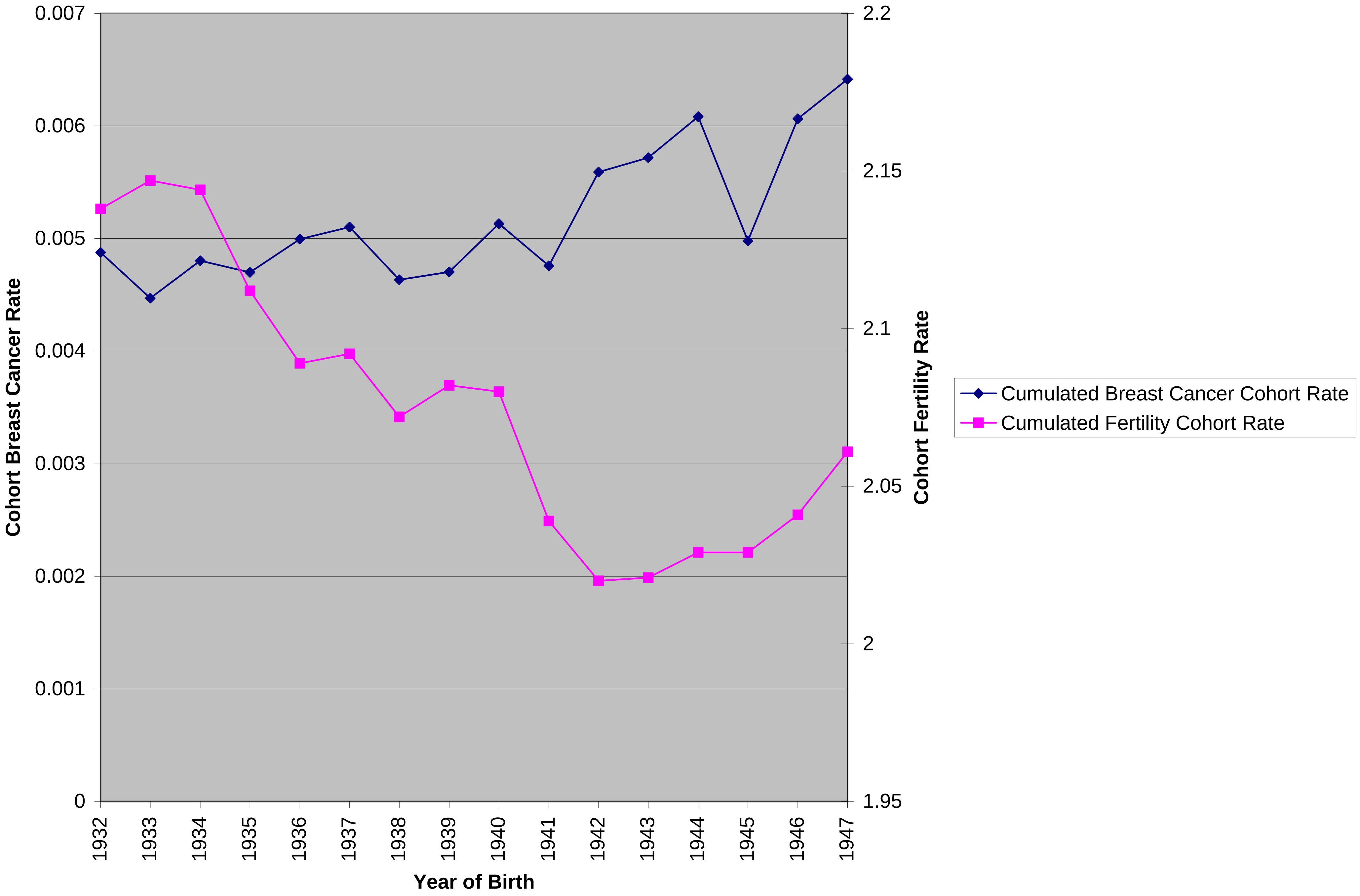

Figure 30
The Czech Republic. Trends in Parous vs. Nulliparous Abortion Cases.