

**Screening mammography (SM) has led to the diagnosis of breast cancer in more than a half million women in the U.S. during the past 30 years.**

**U.S. Breast Cancer Incidence and Stage Distribution Since 1975 Disclose Little to No Benefit of Screening Mammography (SM)**

**Archie Bleyer, MD**

**St. Charles Health System, Central Oregon**

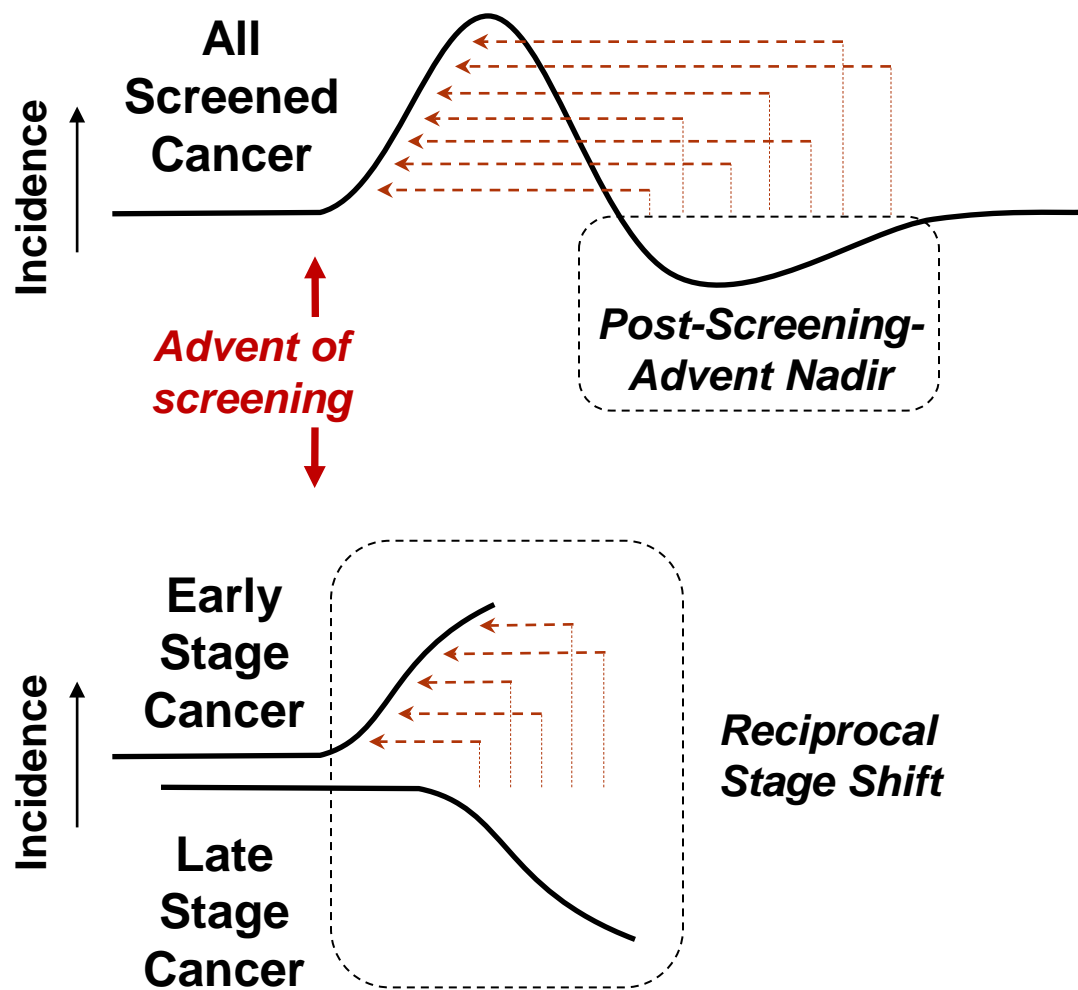
**By now, our country's breast cancer incidence trends should demonstrate some evidence for SM benefit. From an incidence and stage analysis perspective, there is no evidence for benefit in women below age 50, and marginal benefit in older women. Our national data indicate that a very large majority of women with breast cancer detected by SM are over-diagnosed and over-treated.**

## **Epidemiologic Evidence for the Failure of Screening Mammography (SM)**

**The primary purpose of disease screening is to detect earlier disease that results in better outcomes. For cancer, this may be either improved survival or less therapy. Screening that is successful at detecting early disease “pulls” cases out of the future, increases the incidence transiently since the cases detected earlier and thereby not detected later, which leads to a subsequent temporary decrease in incidence (Fig. 0, upper panel). By diagnosing disease earlier, fewer persons are detected to have advanced disease later. By definition, every case of cancer that is diagnosed early means one less more with advanced disease. Thus, successful SM should not only result in increased incidence of early stage, but also and more importantly a decrease in advanced disease, as shown in the lower panel of Fig. 0 (lower panel).**

Fig. 0

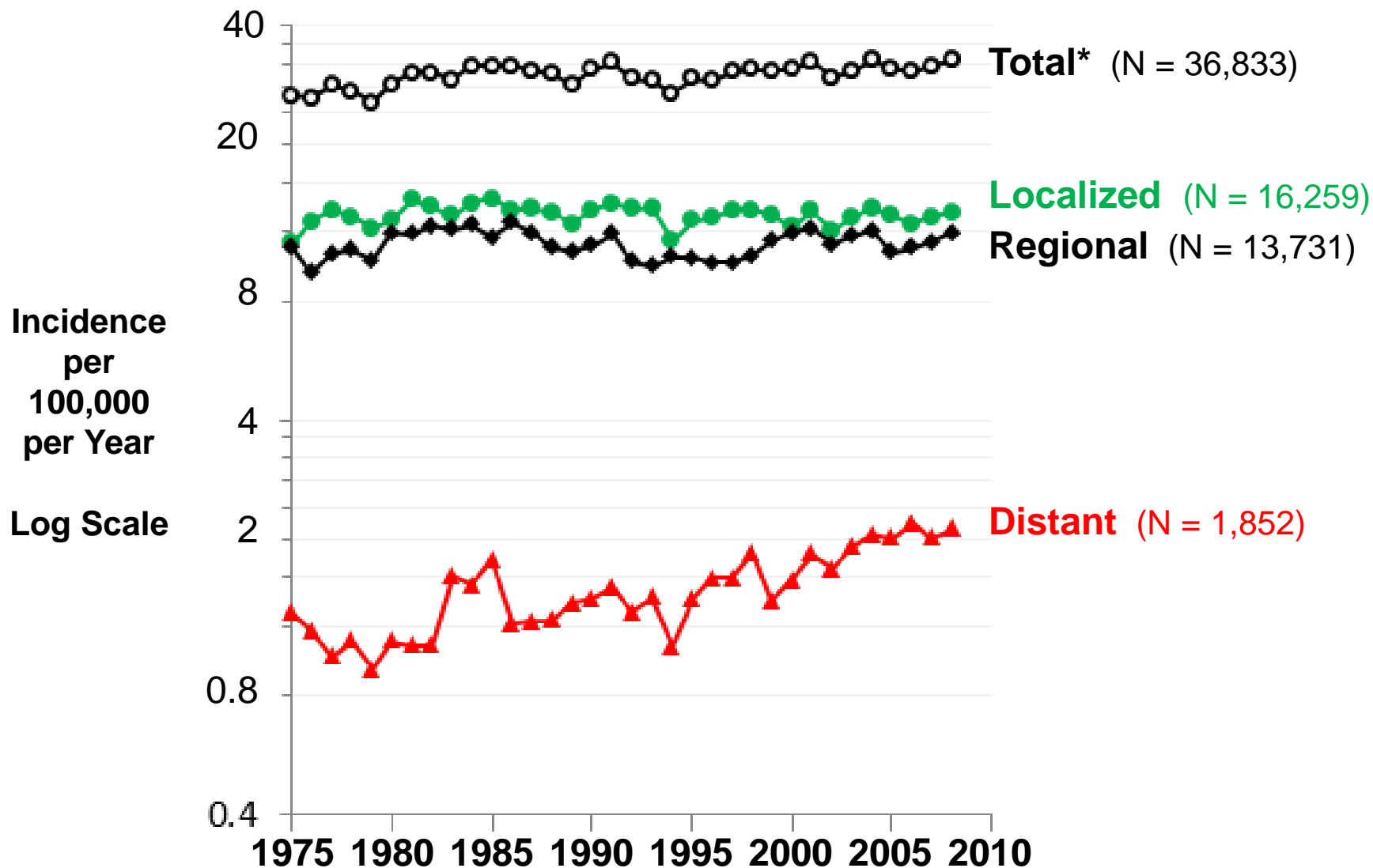
# Expected Trends in Incidence and Stage Distribution with a Successful Cancer Screening Program



**SM Markedly Increased Breast Cancer Incidence but Subsequently Has Not Led to an Expected Reduction in Incidence**

**1975-2008**

**Fig. 1 Annual Incidence from 1975 to 2008 of Breast Cancer in Women Younger than 40 Years by Extent of Disease\***



\*SEER9; Age adjusted to the 2002 U.S. Standard Population (19 age groups – Census P25-1130) Standard

## **Stable Incidence of Breast Cancer in Unscreened Population**

**The incidence of local and regional breast cancer in women less than 40 years of age has been stable since 1975 (Fig. 1).\* Since this population did not undergo screening mammography (SM), a reasonable assumption is that incidence changes in older women are more likely due to SM since a majority of them have undergone SM after it's introduction in the early 1980s.**

\*Distant disease at diagnosis has increased in younger women ( $p < 0.0001$ ), a new finding under investigation.

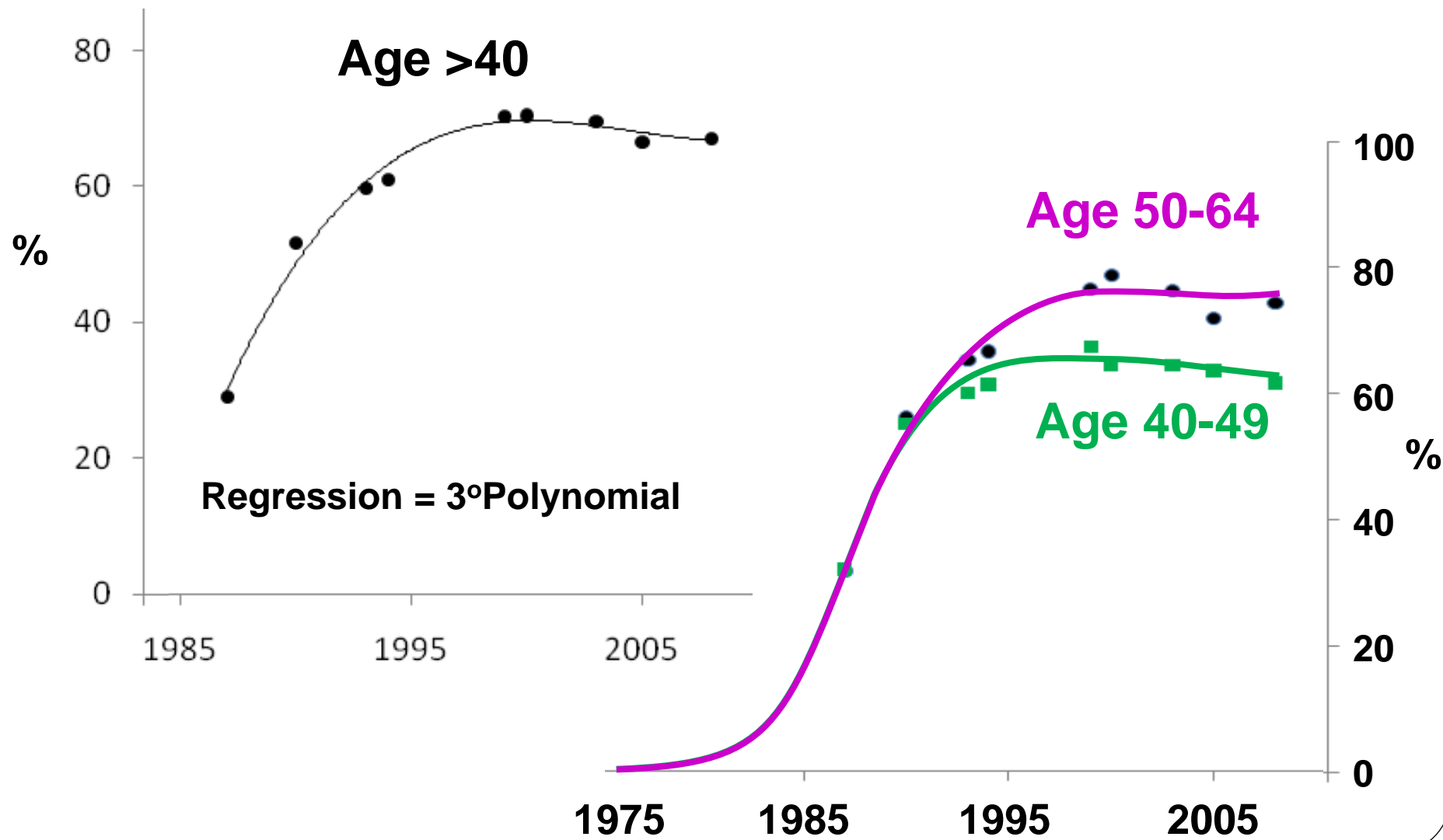
## **U.S. SEER Analysis of Breast Cancer Incidence, 1975-2007**

**It has been more than 30 years since the widespread introduction of screening mammography (SM) in the U.S., which should be a sufficiently long interval to evaluate the national impact of SM on the incidence of breast cancer by era and stage of disease.**

**The proportion of women over 40 of age who underwent SM increased dramatically in the 1980s, reaching 60% by 1990 and 70% by 1995, after which the proportion declined to steady state of 65% (Fig. 2, left panel). Women 40 to 49 years of age have had lower use of SM of 60-65% compared to 50 to 64 year-olds at 70-75% (Fig. 2, right panel).**

**In females <40 years of age, in whom SM was not performed, the incidence of early breast cancer has been steady for the last three decades (Fig. 1).**

**Fig. 2 Proportion of Women in the U.S. >40 Years of Age Undergoing Screening Mammography**  
Age Adjusted, 1975-2008





# **U.S. SEER Analysis of Breast Cancer Incidence, 1975-2008**

## **Conclusion**

**Women over age 40 can be assessed for incidence trends that occurred after SM was routinely recommended in the early 1980s and nationally implemented in more two-thirds of all women in this age group by 1995 and has been above this proportion since (Fig. 2).**

## **Correlation of SM with Breast Cancer Incidence**

**During the 1980s following the advent of SM, the incidence of breast cancer in females older than 40 increased by more than 50% within less than a decade (Figs. 3 and 4). During the next two decades, the incidence remained elevated.**

**Fig. 3 Annual Incidence of All Breast Cancer in Females Age 40+, SEER9, 1975-2008**

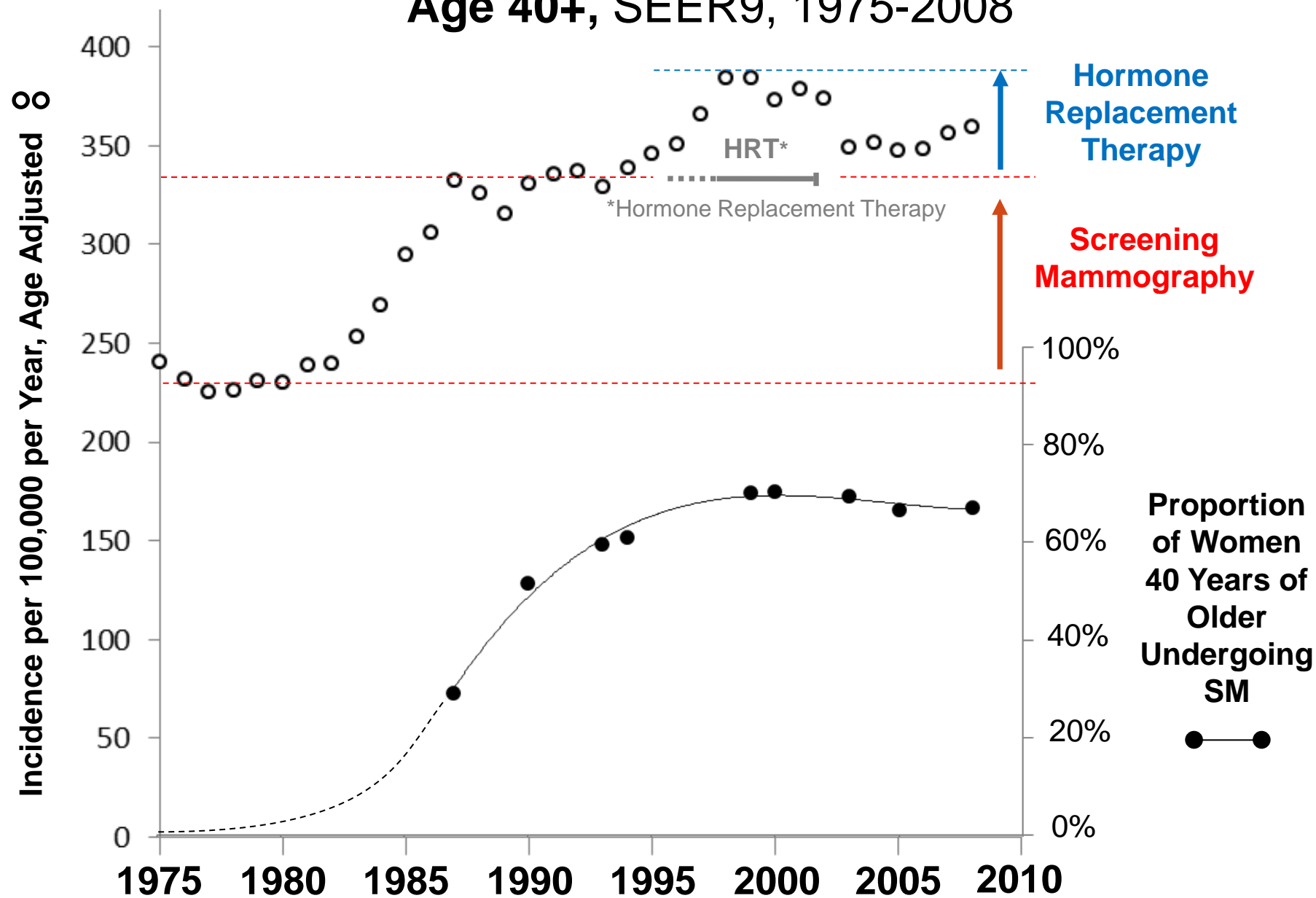
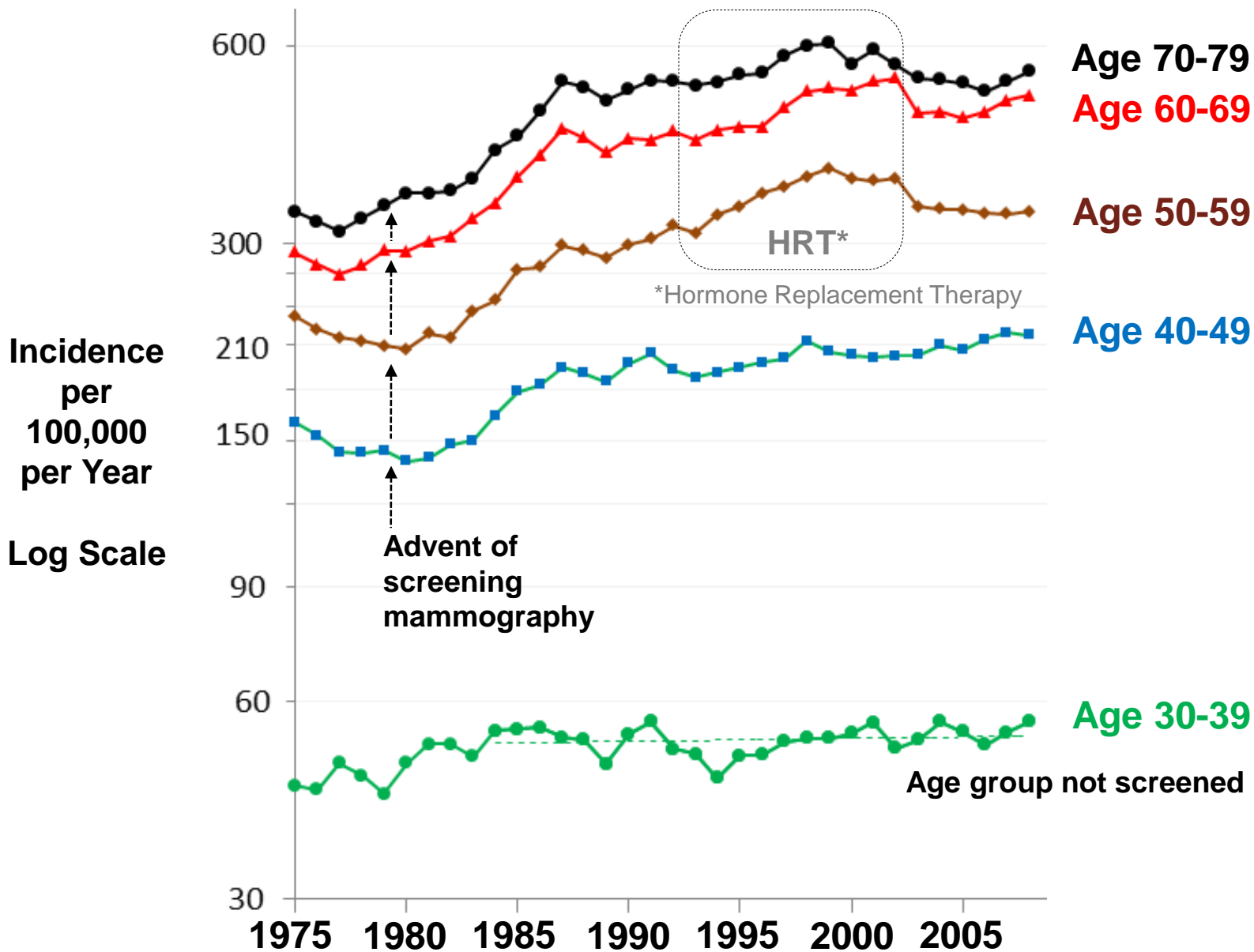


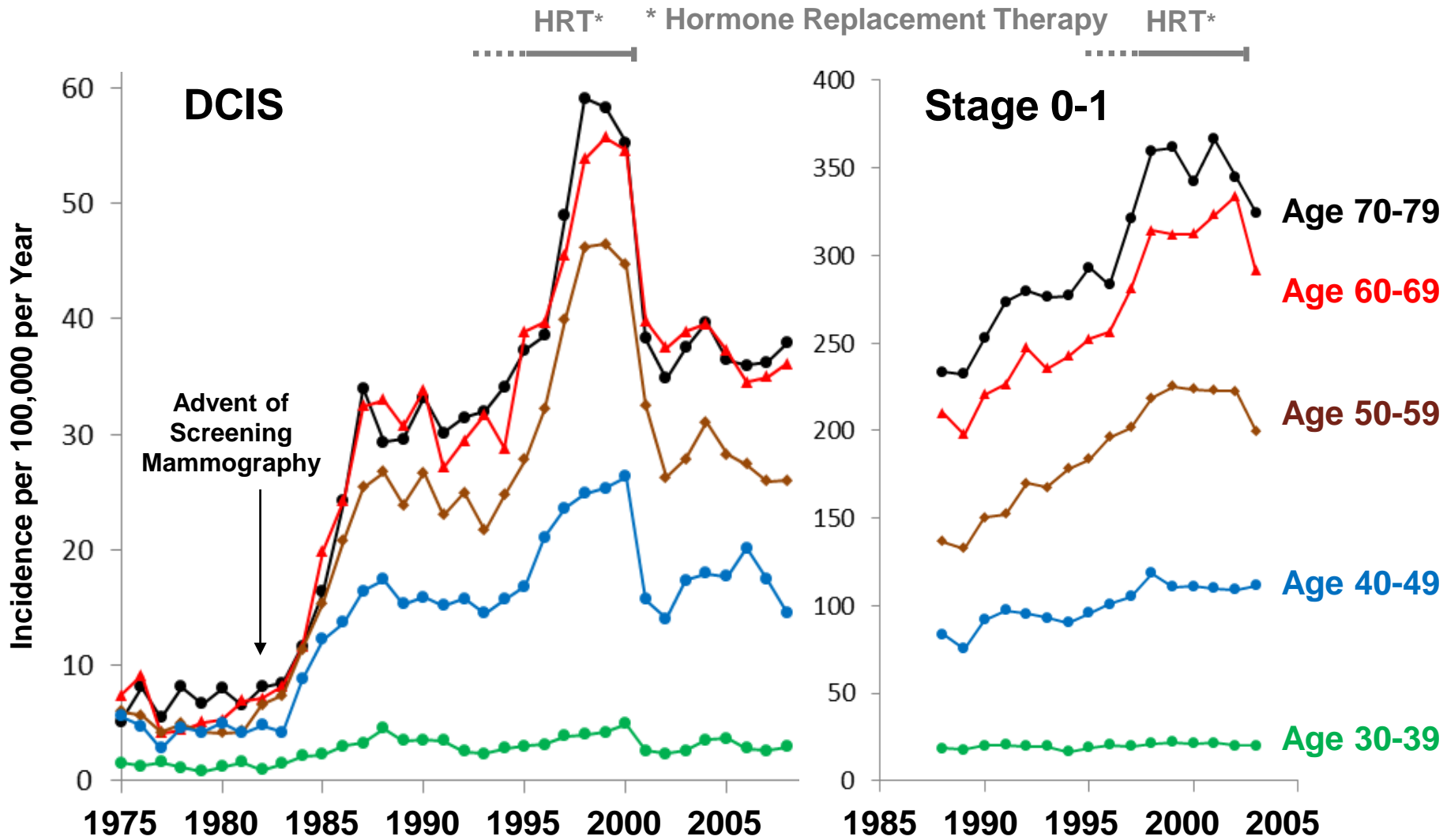
Fig. 4

# Annual Incidence of Breast Cancer in Females by 10-Year Age Intervals, 1975-2008, SEER9



**All of the increase in incidence can be accounted for by the increase in stage 0 and 1 disease including ductal carcinoma in situ (DCIS) (Fig. 5). During the 1980s, the incidence of stage 0 and I increased by 41% to 56% in women 40- to 74- years of age (Fig. 5, right panel) but did not change in younger women who were not screened. The incidence of DCIS, the earliest stage of breast cancer, increased 4 to 5 fold in less than a decade after SM was implemented, and increased transiently during the HRT era (Fig. 5, left panel). As with all breast cancer, a post-SM nadir of incidence that is less than the pre-SM level is not apparent in early breast cancer during the two decades since the initial peak (Fig. 5, left panel).**

**Fig. 5 Annual Incidence of Early Breast Cancer in Women by 10-Year Age Intervals, 1975-2008, SEER9**

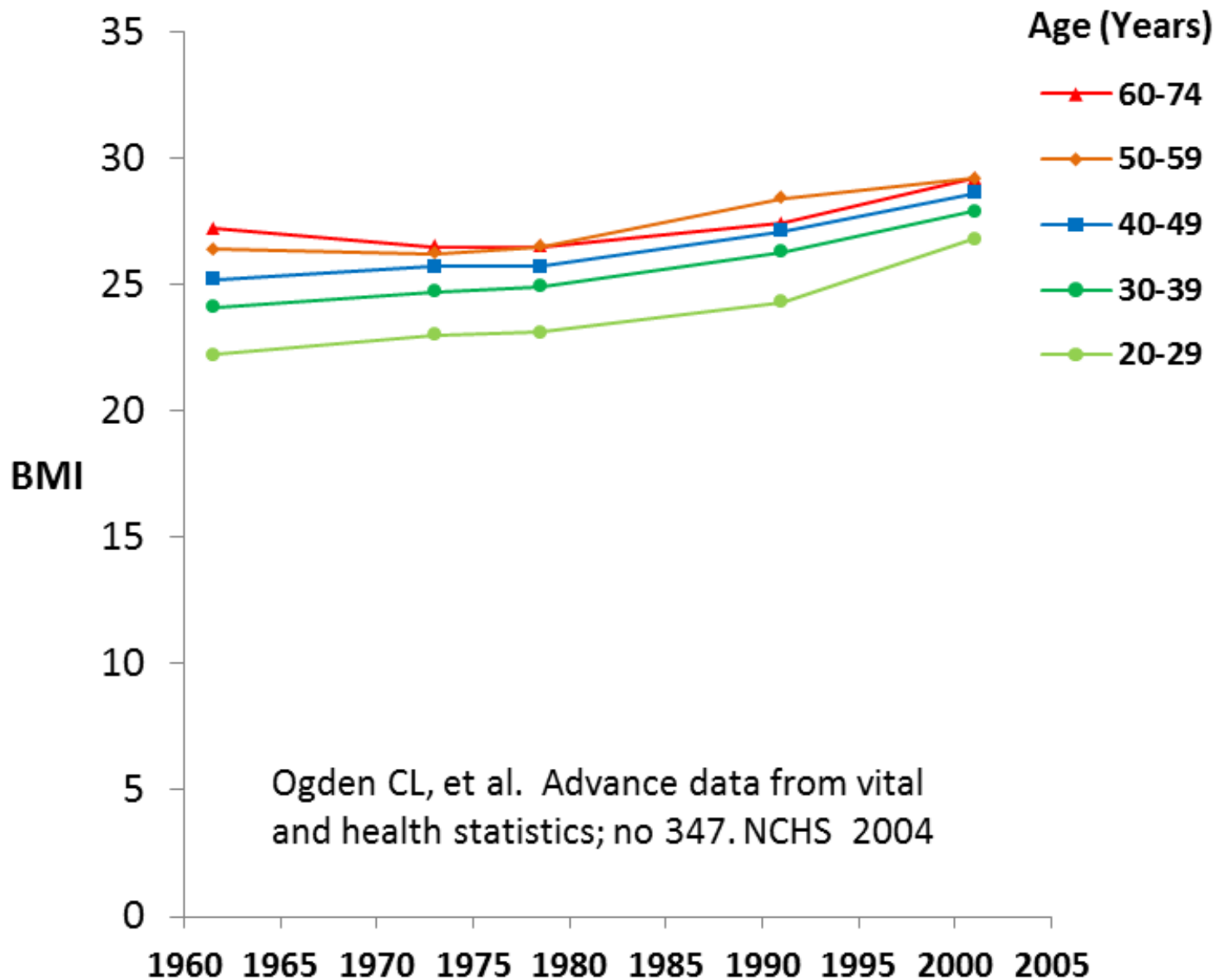


\*SEER9; Age adjusted to the 2002 U.S. Standard Population (19 age groups – Census P25-1130) Standard

**The lack of a decline in incidence during the three decades after the advent of SM may have been prevented by the increasing obesity of our people is associated with an increased incidence of post-menopausal breast cancer or by hormone replacement therapy (HRT) that was prevalent during the 1990s.**

**The absolute rate and temporal trend of obesity epidemic (Fig. 6) however appears too gradual and of more recent impact than the trend patterns of breast cancer incidence.**

**Fig. 6 Mean Body Mass Index (BMI) Trend in U.S. Women 1960-2002**



**HRT was first applied in the mid 1990s and within a few years was associated with an increased incidence of breast cancer and when HRT was widely discontinued in 2002-2003 the incidence rapidly decreased (Figs. 3-5).**

**In women 40- to 49-years of age (Fig. 7), the increase in breast cancer incidence attributable to SM was similar but there was less change during the HRT era. This corresponds to less usage of HRT in this age group and affirms that the transient increase in breast cancer incidence during 1995-2003 in older women was due to HRT.**

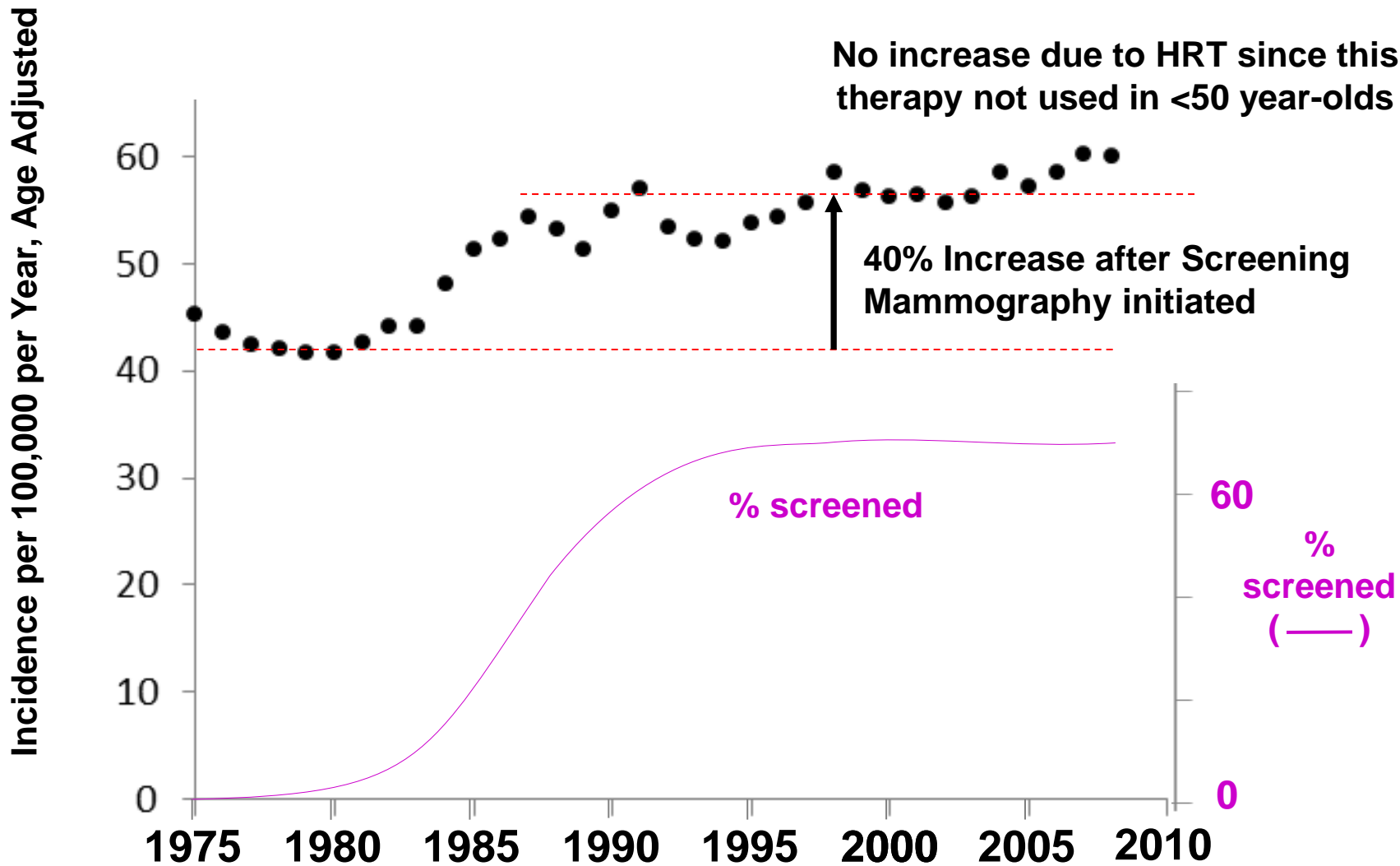
**In women <40 years of age, in whom neither SM nor HRT were applicable, the incidence of breast cancer has no evidence for the incidence peaks of the older age group in which SM or HRT were applied (Figs. 3-5).**



**The Breast Cancer Surveillance Consortium (4) and a Canadian group (5) reported data that indicates HRT effect had essentially leveled off by 2006. The post-HRT peak incidence level is consistent with increased detection of breast cancer due to SM and not to HRT.**

**The post-HRT plateau in breast cancer incidence at essentially the same level it was before the HRT era indicates that the SM 'plateau' in increased incidence has persisted for at least 20 years**

**Fig. 7 Annual Incidence of All Breast Cancer in Females**  
**U.S. SEER9, 1975-2008**  
**Age <50**



## **Conclusions: Overall Breast Cancer Incidence**

- 1. Nearly all of the 30% increase in incidence of breast cancer in the U.S. during the 1980s was due to SM.**
- 2. Assuming that 90% of the increase was due to SM and that 70% of women over 40 have utilized SM, the number of women whose breast cancer was detected by SM between 1985 and 2008 may be estimated to be 467,000 nationally and 121,000 in the SEER13 registry.**
- 3. By now, this large number of SM-detected cancers should have resulted in a trend toward resumption of the pre-SM era overall incidence.**
- 4. For more than 2 decades after SM increased the incidence of early breast cancer, there has been evidence for a decline in incidence.**
- 5. From an ecologic perspective, SM in the U.S. has yet to achieve the primary purpose of earlier detection.**

## **Conclusions: Early Breast Cancer Incidence**

**During the 1980s, the incidence of DCIS, the earliest stage of breast cancer, more than quadrupled within less than a decade after SM was implemented (Fig. 5). The incidence of DCIS also increased transiently during the HRT era (Fig. 5).**

**For more than two decades since the initial incidence peak, there has been no evidence for any of the post-peak pattern that either all or early breast cancer was expected with successful screening (Fig. 0, upper panel).**

### **Conclusions**

- 1. The dramatic surge in DCIS cases as a direct result of SM has not been associated with a post-surge decline.**
- 2. SM appears to be leading to diagnosis of new cases of “cancer” that do not need to be detected.**

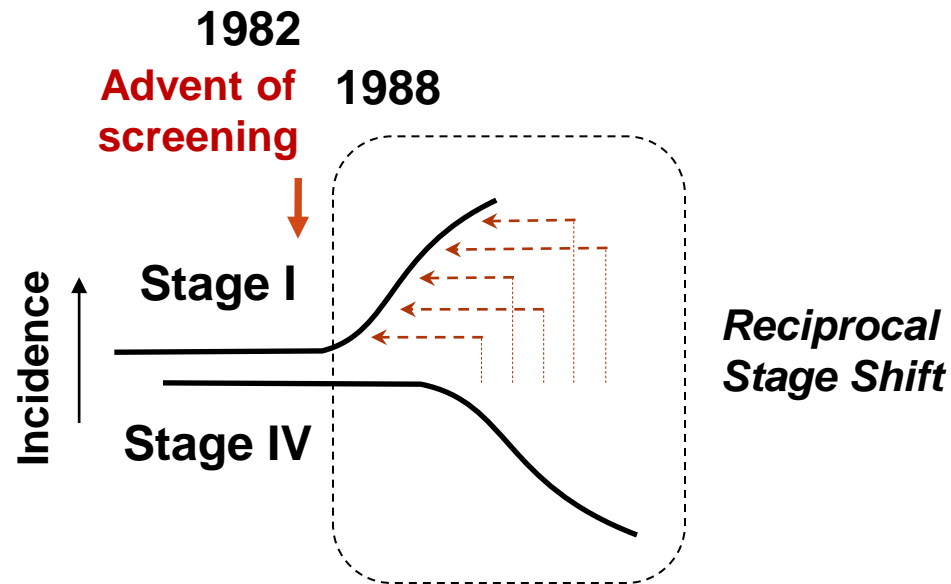
**Screening Mammography (SM):  
Lack of Expected Stage Shift Effect and  
Ecologic Evidence for Overdiagnosis**

**1975-2008**

# Screening Mammography (SM) and Lack of Effect on Stage Shift, 1988-2008

## Background

In theory, the 121,000 women in the SEER registry who were detected to have earlier breast cancer should have by now provided a reciprocal reduction in subsequent women diagnosed with advanced cancer (Figure).



# Screening Mammography (SM) and Effect on Stage 1975-2008

## Methods

All SEER data was obtained via SEER\*Stat (1) applied to the April 2011 release of SEER data (2) in June 2011.

Extent of disease at diagnosis was converted from Collaborative Stage (CS) for 2004+ and Extent of Disease (EOD) prior to that with the following definitions (3):

- *In situ* – ductal and non-ductal carcinoma in situ
- *Localized* – invasive cancer confined to the organ of origin
- *Regional* – metastasis outside of and adjacent to or contiguous with the organ of origin
- *Distant* – extension of metastasis to organs not adjacent to the organ of origin

# Screening Mammography (SM) and Effect on Stage 1988-2008

## Methods (Continued)

In 1988, SEER applied the American Joint Commission on Cancer (AJCC) 3<sup>rd</sup> edition staging system. In 2004, the AJCC used by SEER was replaced by the 6<sup>th</sup> edition.

Breast cancer incidence according to AJCC 3<sup>rd</sup> edition evaluated from 1988 to 2003 with the SEER9 database and from 2004 to 2008 in the SEER18 database with AJCC 6<sup>th</sup> edition. Each age group was age-adjusted to the 2000 US Std Population (19 age groups - Census P25-1130) standard.

Stage 0 breast cancer, *ductal carcinoma in situ* (DCIS), was included in this analysis since these cancers are treated with surgery, radiation and if the cell has certain type of receptor, either intravenous chemo-therapy or a minimum of 5 years of hormonal therapy.



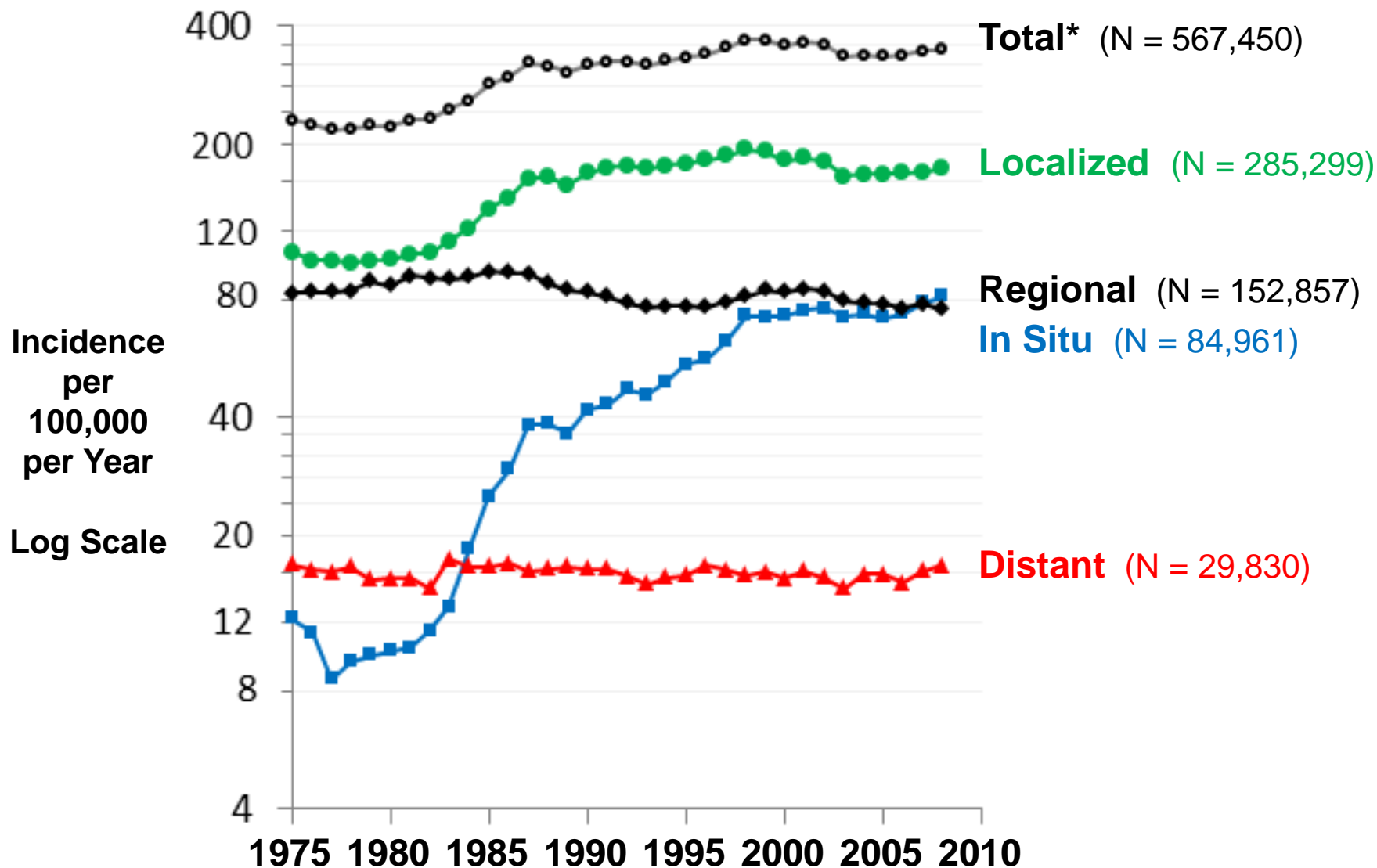
# **Screening Mammography (SM) and Effect on Stage 1988-2008**

## **Results**

**Figure 5 shows the increase in early stage (stage 0 + I and DCIS) in women over 40 or more years of age since the advent of SC. In just 14 years, the increase exceeded 56% in 50-74 year-olds and 40% in 40-49 year-olds. In younger women, in whom SM was not applied, there was no change in the incidence of Stage 0 and I (Fig. 5, lowest curve).**

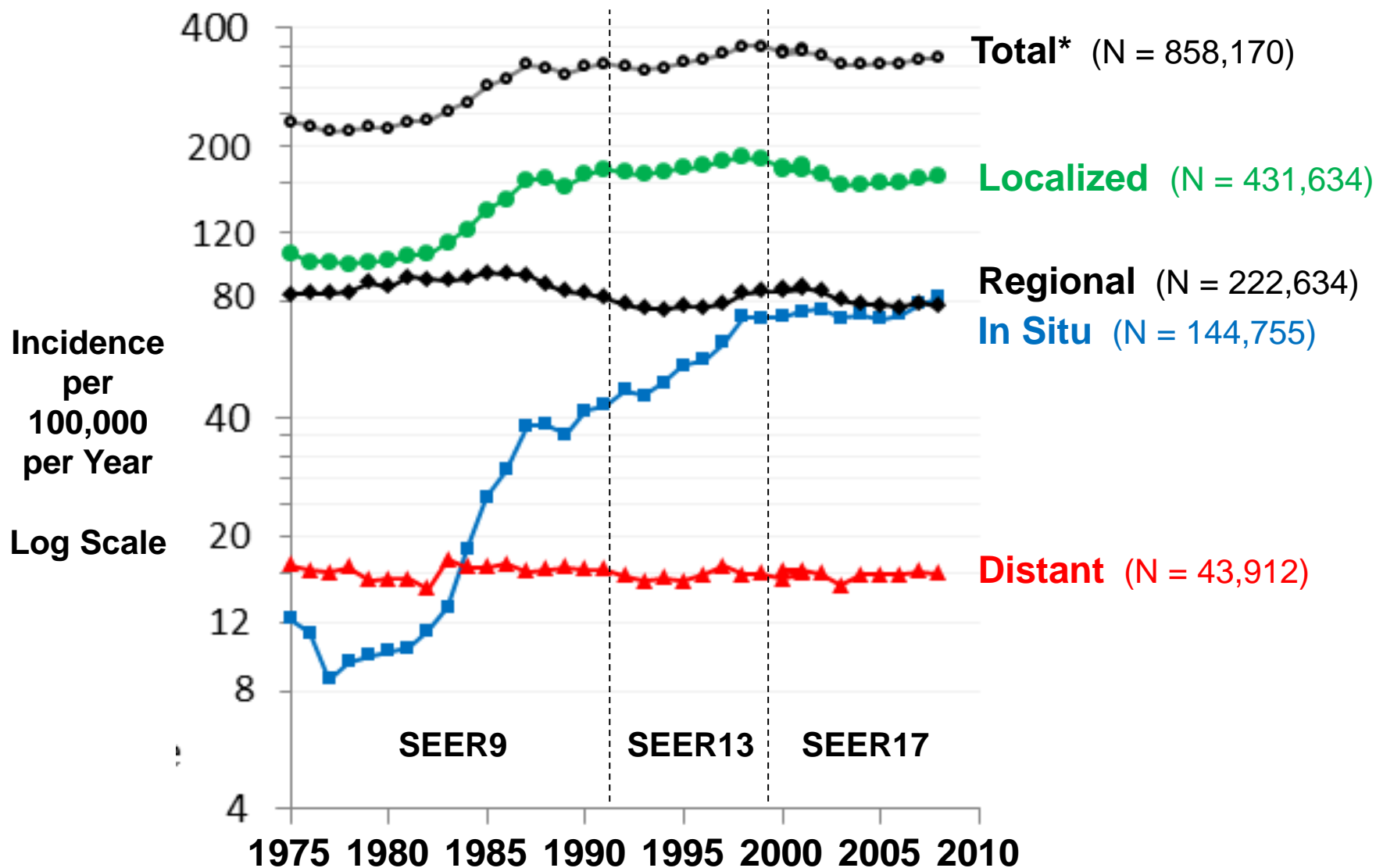
**Figures 8a and 8b depict the incidence of breast cancer in women 40 years of age and older from 1975 to 2008 by the extent of disease at diagnosis and SEER registry (Fig. 8a SEER9 only and Fig. 8b SEER9 for 1975-1991, SEER13 for 1992-1999 and SEER17 for 2000-2008).**

**Fig. 8a Annual Incidence of Breast Cancer in Women  
Age 40 Years and Older from 1975 to 2008 by Extent of Disease\***



\*SEER9; Age adjusted to the 2002 U.S. Standard Population (19 age groups – Census P25-1130) Standard

**Fig. 8b Annual Incidence of Breast Cancer in Women  
Age 40 Years and Older from 1975 to 2008 by Extent of Disease\***



\*Age adjusted to the 2002 U.S. Standard Population (19 age groups – Census P25-1130) Standard

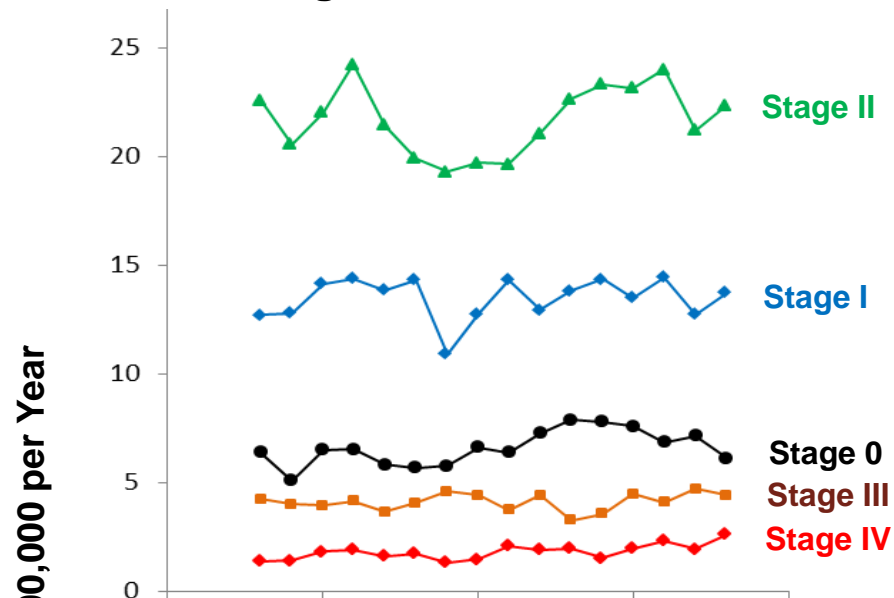
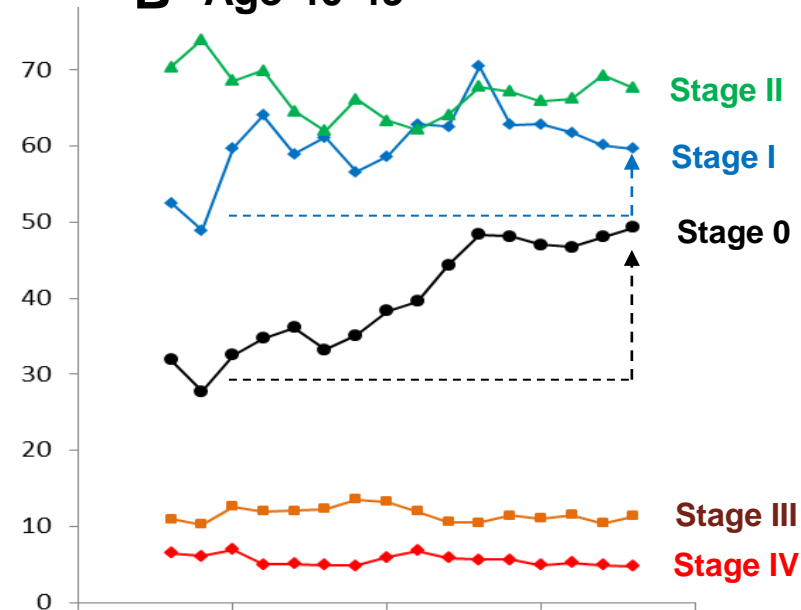
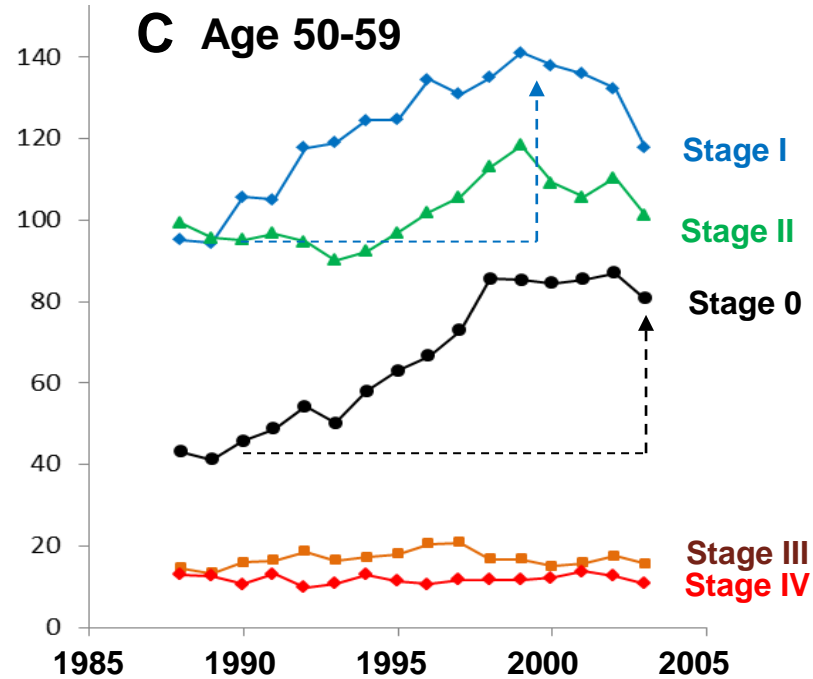
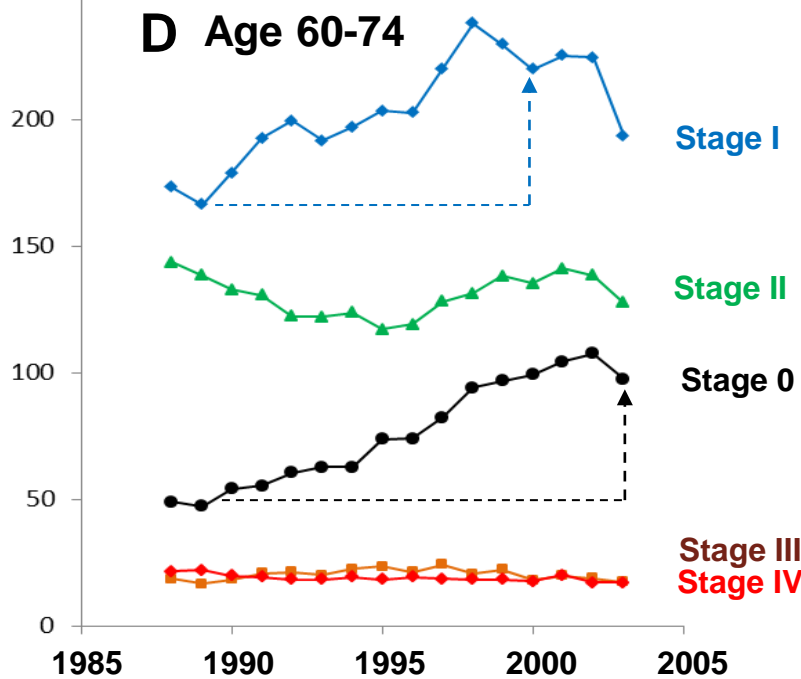
# **Screening Mammography (SM) and Effect on Stage 1988-2008**

## **Results (continued)**

**The incidence of in situ and localized disease increased from 10 to 80 cases and from 100 to 180 cases per 100,000 per year, respectively, between 1980 and 1998.**

**A slight reduction in regional disease but no reduction in distant disease is apparent during the escalation in insitu and localized disease**

**Figure 9 shows the incidence of breast cancer in women from 1988 to 2003 by stage (AJCC3) and age.**

**Fig. 9****A Age 30-39****B Age 40-49****C Age 50-59****D Age 60-74**

# **Screening Mammography (SM) and Effect on Stage 1988-2003**

## **Results (continued)**

**The incidence of stage 0, I, II, and III breast cancer has been stable since 1988 among 30-39 year-olds, in whom neither screening mammography (SM) nor hormone replacement therapy (HRT) has been applied (Figs. 9A). [Stage IV has increased in this age group (Fig. 9A).]**

**In women more than 40 years of age, the incidence of stage 0 and I breast cancer has steadily increased since 1988 as SM increased in the age group, but without any evidence for a commensurate decrease of stage II, III or IV cancers (Figs. 9B,C,D). In women 60 to 74 years of age, there was a slight reduction in the incidence of stage III breast cancer but no change in the incidence of stage IV breast cancer (Fig. 9D).**

# **Screening Mammography (SM) and Effect on Stage 1988-2008**

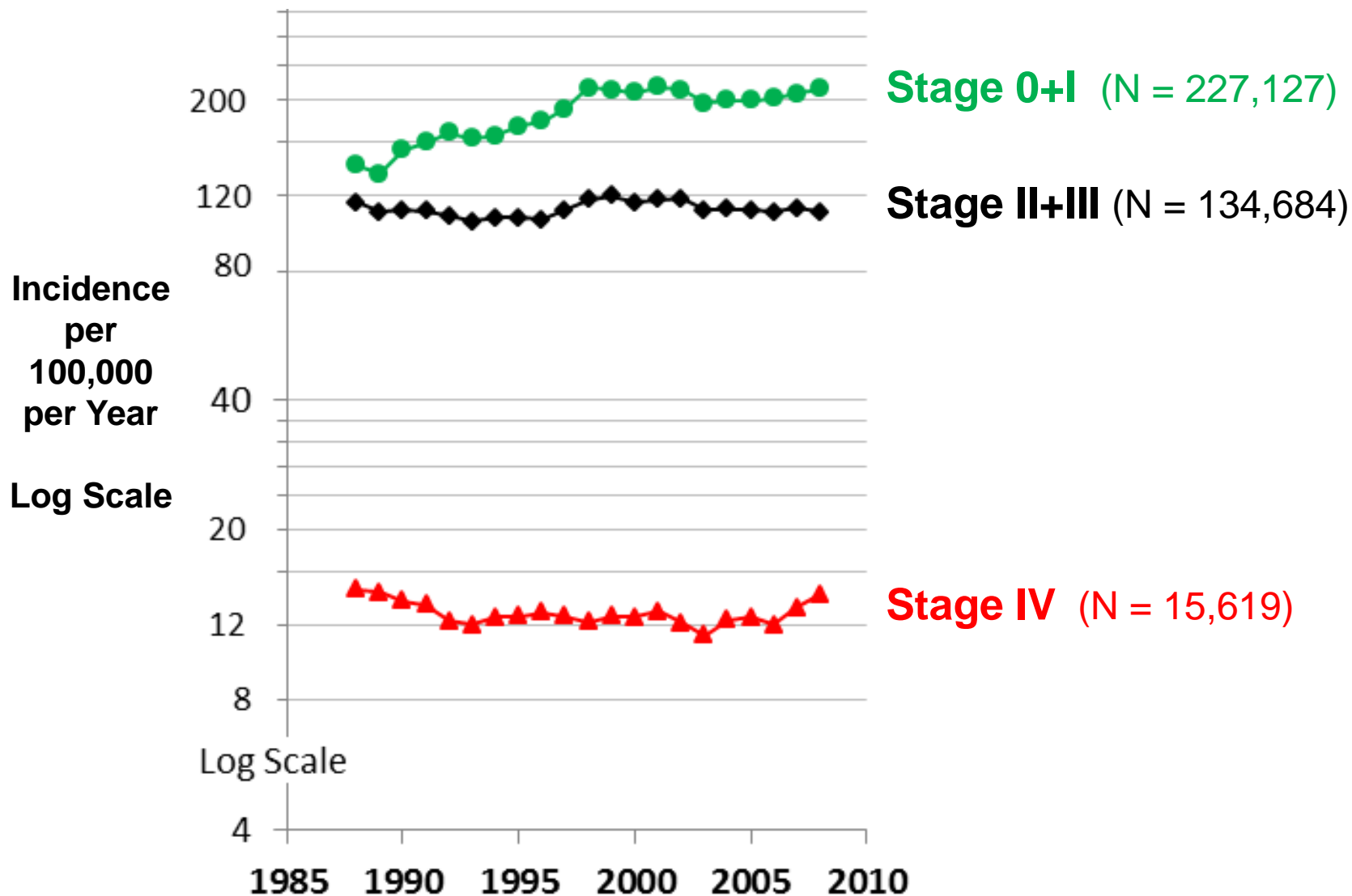
## **Results (continued)**

**Figure 10 shows the annual incidence of stage 0+I, II+III and IV breast cancer from 1988 to 2008 in women 40 years of age and older. The ordinate is a log scale and the data for 1988-2003 and 2004-2008 are based on AJCC3 and AJCC6, respectively.**

**There is no evidence over two most recent decades of SEER surveillance of a reduction in stage II, III or IV despite the increase in stage 0 during the first of the two decades from 135 to 215 new cases per 100,000 per year.**

**Fig. 10**

## Annual Incidence of Breast Cancer in Women from 1988 to 2008, Age 40+, by Stage\*



\*SEER9; Age adjusted to the 2002 U.S. Standard Population (19 age groups – Census P25-1130) Standard



## **Discussion**

**Some evidence for the reciprocal effect of decreased incidence of late stage as a result of increased detection of early stage is apparent in SEER data in women 60- to 74 years of age. The benefit appears to be limited to stage III and is not apparent for stage IV however.**

**Otherwise there is no evidence for a reciprocal effect in 40 to 59 year-olds despite a more than 50% increase in detection of early cancer and despite a two decade (1988-2008) opportunity for benefit to be realized.**

**Depending on how long it takes in individual patients for breast cancer to progress from early to late stage disease, some women diagnosed in their 50s with early stage disease may have contributed to the slight decline in the incidence of advanced stage disease observed in women of age 60 or more.**

## **Discussion (continued)**

**The doubling time of tumor growth has been studied more thoroughly in breast cancer patients than in patients with any other type of cancer. Population mean doubling times measured by with imaging techniques (mammograms, CT scans, ultrasound and MRI) or by clinical palpation have been reported to be in the range of 6 months and inversely proportional to age (6,7).**

**The temporal reciprocity in 60- to 74-year old women of an increase in stage 0-I incidence and a parallel decrease in stage III incidence suggests that progression of breast cancer from early to advanced disease occurs within a few, and not many, years.**

**Thus it is unlikely that untreated breast cancer in women <55 years of age would not be clinically apparent until sometime between age 60 and 74.**

# **Conclusions: Primary & Secondary**

**2011**

# Primary Conclusions

From an epidemiologic/ecologic perspective:

- 1. SM has had no apparent national benefit in 40- to 59-year-olds and marginal benefit in 60-74 year-olds.**
- 2. A small proportion of 60- to 74-year-old women and possibly some women in their late 50s have had earlier detection of stage III breast cancer as a result of SM but not of what otherwise would have been stage IV or distant disease.**
- 3. The vast majority of stage 0 and I tumors that SM has been detecting in 40- to 49-year-olds did not need to be diagnosed or treated (overdiagnosis, overtreatment) since they did not progress to more advanced, clinically detectable disease.**
- 4. Most SM-detected tumors in 50- to 59-year-olds probably are probably also over-diagnosed.**

## **Secondary Conclusions**

- 1. The temporal reciprocity in 60- to 74-year old women of an increase in stage 0-I incidence and a parallel decrease in stage III incidence suggests that progression of breast cancer from early to advanced disease occurs within a few, and not many, years.**
- 2. Incidence data and trends can be used to assess cause and effect, as well as benefits and deficits of SM.**
- 3. The USPSTF recommendation to discontinue routine SM in women <50 years of age is supported by the national breast cancer incidence trends.**
- 4. The analyses performed in this study suggests that the same recommendation may apply to 50-54 year-olds.**
- 5. A similar set of conclusions have recently been published for PSA screening and prostate cancer (8).**

# References

1. <http://www.seer.cancer.gov/seerstat>
2. Surveillance, Epidemiology, and End Results (SEER) Program (www.seer.cancer.gov) National Cancer Institute, DCCPS, Surveillance Research Program, Cancer Statistics Branch, released April 2011, based on the November 2010 submission
3. [http://seer.cancer.gov/seerstat/variables/seer/yr1973\\_2007/lrd\\_stage](http://seer.cancer.gov/seerstat/variables/seer/yr1973_2007/lrd_stage).
4. 20. Farhat GN, Farhat GN, Walker R, Buist DS, Onega T, Kerlikowske K. Changes in invasive breast cancer and ductal carcinoma in situ rates in relation to the decline in hormone therapy use. *J Clin Oncol* 2010;28[35, Dec 10]:5140-5146.
5. De P, Neutel I, Olivotto I, Morrison H. Breast cancer incidence and hormone replacement therapy in Canada. *J Natl Cancer Inst.* 2010;102(19):1489-95.
6. Bailey SL, Sigal BM, Plevritis SK. A simulation model investigating the impact of tumor volume doubling time and mammographic tumor detectability on screening outcomes in women aged 40-49 years. *JNCI.* 2010 Aug 18;102(16):1263-71. Epub 2010 Jul 27.
7. Vieira IT, de Senna V, Harper PR, Shahani AK. Tumour doubling times and the length bias in breast cancer screening programmes. *Health Care Manag Sci.* 2011 Jun;14(2):203-11. Epub 2011 Mar 29.
8. Crosswell J, Kramer BS, Crawford ED. Screening for Prostate Cancer With PSA Testing: Current Status and Future Directions. *Oncology* 2011;25[6]:1-13