Chapter 9
Cancer Screening in the U.S. and Europe: Policies, Practices, and Trends in Cancer Incidence and Mortality

Krista Garcia and Eileen M. Crimmins

Introduction

Population-based data are increasingly used to elucidate the burden of cancer worldwide. Incidence and mortality data from regional and national cancer registries should allow researchers to monitor trends and disparities in cancer occurrence, survival, and mortality in populations and subgroups of the population and to evaluate the effectiveness of screening for cancers amenable to early detection and treatment. Given that the primary purpose of screening is to reduce the number of deaths attributable to cancer, cancer mortality is assumed to be the most important indicator of the effectiveness of screening and the most basic measure of progress against cancer (Hakama et al. 2008; Jatoi and Miller 2003). In setting screening policy, the deaths saved by screening, however, must be weighed against any adverse effects of screening resulting from over identifying or over treating cases, as well as monetary costs.

Recent studies on cancer in the United States (U.S.) and Europe show an overall decline in cancer mortality in recent years; however the magnitude of the decline and current mortality rates are variable across Europe and between the U.S. and other high-income European countries (Jemal et al. 2010; La Vecchia et al. 2010; Crimmins et al. 2010). Declines in screened cancers including breast, prostate, and colorectal cancers have played important roles in the reduction in overall cancer mortality (Jemal et al. 2010; Karim-Kos et al. 2008; Boyle and Ferlay 2005b; Baade et al. 2004; Botha et al. 2003; Quinn et al. 2003). Screening, along with improved diagnostic methods, and therapeutic advances are thought to be responsible for site-specific cancer declines, however the extent to which each of these factors is responsible for the declines remains largely unknown and controversial.

K. Garcia (✉) • E.M. Crimmins
Davis School of Gerontology, Andrus Gerontology Center,
University of Southern California, Los Angeles, CA, USA
e-mail: kegarcia@usc.edu

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This paper compares screening policy, screening uptake, and recent trends in cancer incidence and mortality rates in the U.S. and high-income European countries for cancers of the breast, prostate, colon, rectum, and anus among persons aged 50 years and older. As the approaches to screening in the U.S. and Europe have been similar in some, but different in many respects, the comparison allows the outcomes of key differences to be evaluated. We examine mortality trends in two time periods, 1980–1989 and 1990–2005, before and after screening became more widespread, to identify differences in the rate of decline in site-specific cancer deaths across countries with different uptakes of cancer screening. We find that in general, greater declines in mortality coincide with higher uptake of screening, however our results should be interpreted with caution. To conclude, we highlight the challenges and critical issues in this field of research.

Cancer Screening

The aim of cancer screening is to reduce cancer mortality through regular and systematic examinations of asymptomatic persons, so that cancers are detected at earlier stages when they are more responsive to appropriate treatments, thus minimizing the loss of life as well as the social and financial burden of cancer (von Karsa et al. 2008). While many of the technologies used for screening are also used for the diagnosis of cancer among those with symptoms, screening refers to the use of tests and exams among those who are not symptomatic as part of preventative health care. There are risks, as well as benefits, associated with screening and early detection. While screening can identify cancers that will become symptomatic and can cause death, screening also identifies slow-growing and indolent tumors that may result in the diagnosis and treatment of a "cancer" that would otherwise not go on to cause symptoms or death if undetected or untreated (Welch and Black 2010). It is important to note that the term "cancer" represents a continuum of disease, ranging from noninvasive to invasive carcinoma, and screening techniques may detect both of these disease entities as well as noncancerous benign tumors and lesions (Nelson et al. 2009).

Public health policies related to cancer screening have been integrated into preventive health care in many countries; however screening guidelines for particular cancers vary considerably across countries. Screening policies and methods, while generally based on scientific analysis and evidence-based recommendations, can also reflect economic considerations. In Europe, screening guidelines and programs are strictly based on findings from randomized controlled trials (RCT) that have demonstrated a significant reduction in cancer mortality as a result of screening (Hakama et al. 2008). In the U.S., screening guidelines have also been based on observational and diagnostic accuracy studies, rather than relying only on experimental evidence from RCTs. For instance, the recommendation for widespread use of the prostate specific antigen (PSA) test in the U.S. as a screening tool for prostate cancer prior to supporting results from randomized trials serves as an example of intuitive screening practices.

Despite widespread use of screening, optimal screening policy remains controversial. For example, in the U.S., revised recommendations by the U.S. Preventive Services Task Force in 2009, to increase the age at which routine screening should begin from 40 to 50 and reduce the frequency of routine mammograms, conflicted with long-standing recommendations by other medical groups and sparked a great deal of controversy. While RCTs are generally considered the gold standard for determining a screening modality's effectiveness in reducing mortality from a particular cancer, conflicting and inconclusive results among RCTs have generated much debate among the medical community and have created a great deal of confusion among both medical practitioners and the public as to when the benefits of screening outweigh the risk of adverse effects as a result of screening. Another source of confusion is that the mortality benefit of screening not only depends on the type of cancer, but also on age, adding to the difficulty in setting universal sets of screening recommendations.

In the following section we discuss the screening modalities generally used to detect breast, prostate, and colorectal cancer and their effectiveness in reducing cancer-specific mortality. These are major cancers, with breast cancer responsible for 16.5% of all cancer deaths among women, prostate cancer responsible for 9.2% of all cancer deaths among men, and colorectal cancer responsible for 11.2% of all cancer deaths among men and women in the U.S. and Europe in 2008 (Ferlay et al. 2010). Each of these cancers is amenable to screening but each has different issues related to screening effectiveness in reducing cancer-specific mortality and appropriate screening policy.

Breast Cancer

Breast cancer has an asymptomatic phase that can be identified with various screening techniques including screen film and digital mammography, magnetic resonance imaging (MRI), and ultrasound. Our discussion will focus on mammography. For women at high-risk for breast cancer, MRI may be used as a screening modality (Nelson et al. 2009; Warner et al. 2011), however there are currently no studies investigating its effectiveness in reducing breast cancer mortality. Numerous organizations continue to recommend clinical breast exams as a complementary examination to mammography screening, however self examination is no longer recommended by most organizations (Anees et al. 2007). In two RCTs, no mortality benefit to breast self-examination was found (Semiglazov et al. 2003; Thomas et al. 1997).

Screen-film mammography gained widespread use after its introduction in the late 1980s and is the most extensively studied screening modality. When an abnormal mammographic finding is identified, additional imaging and biopsy for tissue sampling may be recommended to further discriminate cancerous and noncancerous conditions and to classify the lesion in more detail.

Mammography screening guidelines are generally based on the findings from eight randomized trials conducted in the U.S., Sweden, United Kingdom, and Canada.

Findings from these trials show mammography to be effective in reducing mortality from breast cancer by 20 to 35% among average-risk women ages 50–69 (Nystrom et al. 2002; Shapiro 1994). It is estimated that 465 women need to be screened (every 24–33 months), for 7 years in order to save one life over 20 years (Tabar et al. 2004). This estimate translates to 1,499 mammographic examinations needed to prevent one death among average-risk women in the 50–69 age range. Recent research on the effectiveness of mammograms among younger women, those between age 40 and 50, indicates that mammography is much less efficient in this age range (Quanstrum and Hayward 2010). It is estimated that more than 1,900 women between the ages of 40 and 49 years need to be screened in order to save one life from breast cancer during 11 years of follow-up (Nelson et al. 2009). If women in this age range are receiving annual mammograms, this estimate translates to 20,944 mammographic examinations needed to prevent one death, indicating that each mammogram has less than a 1 in 20,000 chance of preventing a death from breast cancer among average-risk women in the 40–49 age range (Quanstrum and Hayward 2010; Goldberg 2010). It is this difference in effectiveness that has resulted in the changing of recommendations for mammography screening among women younger than 50.

There are critical evidence gaps on the effectiveness of mammography in decreasing breast cancer mortality among average-risk women aged 75 years and older (Galit et al. 2007). A randomized controlled trial on the efficacy of mammographic screening in women over age 74 has not been conducted. However, data from two cohort studies (McCarthy et al. 2000; McPherson et al. 2002) and one nested case-control study (van Dijck et al. 1994) suggest that mammography screening among women aged 75 years and older with a reasonable estimated life expectancy may be associated with identification of earlier-stage disease and lower breast cancer mortality (Galit et al. 2007).

The potential harms associated with mammography screening include pain during the procedure, along with anxiety and distress, although these effects are usually transient (Lerman et al. 1991; Ekeberg et al. 2001; Lampic et al. 2001). More serious harms include false-positive results that lead to further diagnostic evaluation and unnecessary treatment. The specificity of a single mammographic examination is 94–97%, indicating that 3–6% of women who do not have cancer undergo further diagnostic procedures (Humphrey et al. 2002). The percentage of women experiencing one false-positive result over time, however, is much higher due to the cumulative risk of multiple examinations from routine screenings (Elmore et al. 1998; Croswell et al. 2009). It is estimated that for every one life saved from breast cancer, approximately 2,000 false-positive mammograms will occur among screened women between the ages of 40 and 49 years (Nelson et al. 2009). Approximately 400 false-positive mammograms will occur among screened women between the ages of 60–69 years. Furthermore, there is a 1–3% increase in the relative risk of developing breast cancer due to the small dose of ionizing radiation received during mammography (Nelson et al. 2009).

Prostate Cancer

Digital rectal examination and the PSA test are the two methods used to screen for prostate cancer. PSA testing was developed in the mid 1980s primarily for physicians to monitor the progression of confirmed prostate cancers before and after cancer treatment. However, by the early 1990s, the PSA test, performed in conjunction with a digital rectal examination, had become the primary method for prostate cancer screening in the U.S. (Cookson 2001).

The test measures the amount of prostate-specific antigen, a protein produced by cells in the prostate gland, in the bloodstream. Elevated levels are associated with tumors in the gland, as well as common non-cancerous conditions such as prostatitis (inflammation of the prostate) and benign prostatic hyperplasia (enlargement of the prostate). PSA levels also tend to increase with age. Test results do not distinguish between cancerous tumors and benign prostate conditions; a biopsy is needed for distinction and classification. The common threshold for biopsy is 4 ng/ml, however varying cut-off values have been adopted to increase the test's sensitivity and specificity (Bangma et al. 2007; Holmström et al. 2009).

PSA testing combined with digital rectal examination is simple, minimally invasive, and readily available. Screening for prostate cancer can result in the detection of small volume, low grade, and organ confined prostate tumors diagnosed at an early stage (Catalona et al. 1991; Postma et al. 2006; Draisma et al. 2006). Diagnosis of early stage virulent tumors is important and can save lives. However, most tumors in the prostate grow slowly, are unlikely to spread, and do not become symptomatic or clinically significant for many years or even decades. For this reason, most men with prostate cancer are more likely to die with prostate cancer than from it (Sakr et al. 1994; Brawley et al. 1998). Based on postmortem studies, over 30% of men who died in their seventh decade with no known history of prostate cancer had detectable malignant cancer in the prostate at autopsy (Sanchez-Chapado et al. 2003; Soos et al. 2005; Hass et al. 2007). Because of the test's high rate of identifying tumors that would not cause mortality, there is concern over the adverse effects associated with additional diagnostic and treatment procedures. Biopsy and treatment following a positive diagnosis can result in morbidity and significant declines in quality of life due to the risks of erectile dysfunction and incontinence (Raaijmakers et al. 2002; Potosky et al. 2000; Wilt et al. 2008).

Scientific evidence of a mortality benefit from prostate screening was sought in two landmark randomized controlled trials: the U.S.-based Prostate, Lung, Colorectal, and Ovarian (PLCO) Cancer Screening Trial and the European Randomized Study of Screening for Prostate Cancer (ERSPC). Despite the assumption that the two trials would clarify the effects of prostate cancer screening, findings of the studies led to different conclusions. The American randomized trial reported no evidence of a mortality benefit to screening with up to 10 years of follow-up (Andriole et al. 2009), while the European trial reported a 20% decline in mortality after 9 years of follow-up (Schroder et al. 2009). The European trial

indicated that 1,410 men would need to be screened and 48 additional cases would need to be treated to prevent one death from prostate cancer (Schroder et al. 2009).

The disparity in results is attributed to differences in the protocol, execution, and contamination levels between the two trials (Pinsky et al. 2010; La Rochelle and Amling 2010). Because screening for prostate cancer has become a regular part of American health care, PSA tests were being received by approximately 50% of the men in the control group of the American trial. In Europe, the PSA test is less commonly used as a screening tool for prostate cancer. Contamination was projected to be 20% in the design stage of the trial, thus the European trial was less affected in its control arm by screening behavior outside of the study. Nonetheless, high usage of the intervention in the control group reduces the effective sample size and statistical power of each study (Pinsky et al. 2010; Boyle and Brawley 2009), weakening ability to reach a valid conclusion about the mortality benefit from screening. Preston (2009) interprets the results from these two trials to indicate that the United States would gain no mortality benefit by expanding PSA testing beyond its already high screening levels, whereas European countries would benefit from an expansion. The debate over prostate cancer screening continues in light of these findings.

Colorectal Cancer

Several screening test modalities are available for colorectal cancer, including fecal occult blood test (FOBt), sigmoidoscopy, and colonoscopy (Atkin 2003). Studies suggest that colorectal cancer has an asymptomatic phase when benign adenomatous polyps develop into early, localized cancers, before further progressing into advanced and potentially fatal cancers. The average time for an adenoma (pre-cancerous polyp) to progress to carcinoma is approximately 10 years, and tests that detect adenomas, such as endoscopy, can be offered less frequently. It is important to note that 90% of adenomas remain benign, and screening for them can result in overtreatment. For the 10% of adenomas that do develop into carcinoma, it takes approximately 2–3 years for an asymptomatic cancer to become symptomatic, thus screen-detected colorectal cancers are typically diagnosed 2–3 years earlier than clinically detected cancers (Atkin 2003).

The FOBt is the most extensively studied screening modality and has been shown in three randomized trials to reduce colorectal cancer mortality by 20–33% (Mandel et al. 1999; Kronborg et al. 1996; Jørgensen et al. 2002; Hardcastle et al. 1996). The FOBt (home-test kit commonly used) is a noninvasive, inexpensive test that involves placing consecutive stool samples onto cards and mailing them to a lab for processing. Investigation of the colon by endoscopy is generally recommended for positive results. Proponents of the FOBt argue that the test is a cost-effective screening modality by reducing the number of endoscopies administered, although endoscopic examinations have greater sensitivity in detecting adenomatous polyps and early cancers compared to stool tests when considered as a single test (Whitlock et al. 2008).

Colonoscopic screening methods are considered to be the gold-standard due to greater sensitivity for detecting adenomas and carcinomas in both the distal and proximal colon, and the ability to remove pathological lesions within a single examination (Zavoral et al. 2009). Despite these advantages, there is currently no published data from multicenter RCTs on the efficacy of colonoscopy screening in reducing colorectal cancer incidence and mortality. However, findings from a controlled, multicenter randomized study on the efficacy of a once-only flexible sigmoidoscopy screen, which can also remove pathological lesions and detect adenomas and carcinomas of the rectum and sigmoid colon where approximately two-thirds of adenomas and cancers are located, suggest that this examination can reduce colorectal cancer incidence by 23% and reduce mortality by 31%, when offered only once between ages 55 and 64 years (Atkin et al. 2010). Based on the data from this trial, 489 people need to be screened by sigmoidoscopy to prevent one death from colorectal cancer after a median of 11 years of follow-up. These findings suggest that sigmoidoscopy may be a more cost-effective population-based screening modality than colonoscopy, because it is a relatively safe procedure that does not require anesthetics and necessitates less time and preparation for patients (Loeve et al. 2000). Although evidence suggests that population-based screening for colorectal cancer is effective, there is still debate over which screening modality is appropriate (Hawkes and Cunningham 2010).

Comparison of Cancer Screening in the U.S. and Europe

The establishment of organized population-based cancer screening programs in the European Union has distinguished European screening practices from that of the U.S., where cancer screening is predominantly opportunistic. In the U.S., screening behaviors and practices generally depend on individual level circumstances such as one's awareness of, decision to seek, and/or access to care and health insurance. Organized screening programs in Europe, however, operate under a standardized system of care in which nationally implemented guidelines chosen by government or health departments define the target population to be invited, the screening method to be used, and the screening interval followed for particular types of cancers (Miles et al. 2004). With over 50 nationwide screening programs for breast, cervical, and colorectal cancer, the Europe Union leads the way in population-based screening; however in the first implementation report in 2003, less than half of the minimum recommended numbers of screenings took place in the EU each year and more than half of the annual volume of screening examinations (59%) were administered outside of population-based programs (von Karsa et al. 2008).

Significant variation in screening test utilization between the United States and Europe and across European countries is observed (Howard et al. 2009; Stock and Brenner 2010; Preston and Ho 2010). Cancer screening in the U.S. is among the highest compared to other countries, with a generally higher prevalence of screening at both younger and older ages (Preston and Ho 2010; Howard et al. 2009; Cutler 2008).

Recent analyses of the risks and benefits of screening have questioned the health and mortality benefits accruing to the aggressive screening practices at older ages in the U.S., resulting in the recommendations against routine screening for breast cancer in women older than 70 years (USPSTF 2009), for colorectal cancer in adults older than 75 years (USPSTF 2008a), and for prostate cancer in men older than 75 years (USPSTF 2008b). Although age-based limits for routine screenings are relatively new in the U.S., many European countries have targeted persons within a specified age range and have used age-based limits since the implementation of population-based screening programs in the late 1980s and early 1990s (Shapiro et al. 1998; Miles et al. 2004). It is important to note that age-based limits for both breast and colorectal cancer screening vary considerably across Europe, and persons outside the age range can request to continue screening in a number of countries (von Karsa et al. 2008; NHSSP 2006).

Screening Policies and Prevalence

Guidelines for cancer screening in the U.S. and Europe generally differ in the methods used for screening and the populations targeted for screening. In this section, we highlight screening policies and guidelines for individual cancers of the breast, prostate, and colorectal in the U.S. and Europe. We discuss how variations in screening policies and guidelines in the U.S. and Europe have translated to differences in screening practices and patterns. Screening prevalence estimates based on data from nationally represented surveys are presented.

Breast Cancer

Screening mammography guidelines in the United States differ from those in Europe. The Council of the European Union recommends biannual mammography screening for women between the ages 50–69 years of age. Conversely, most major U.S. medical organizations and government agencies such as the American Cancer Society, American College of Radiology, and the American Medical Association, have recommend annual mammography screening for women aged 40 years and older; however, the US Preventative Services Task Force and the American College of Preventative Medicine recently updated their guidelines to include annual or biannual screening for women between the ages of 50–69, resembling European guidelines.

Comparing data from the United States and nine European countries, in 2004, the U.S. had the highest percentage (77.7%) of women between the ages 50–64 reporting that they received a mammogram in the past two years (Howard et al. 2009). Although mammography use declines with age, there is greater variation in the percentage of women screened at older ages and the U.S. has by far the highest screening percentage with almost two-thirds of American women aged 75 and over

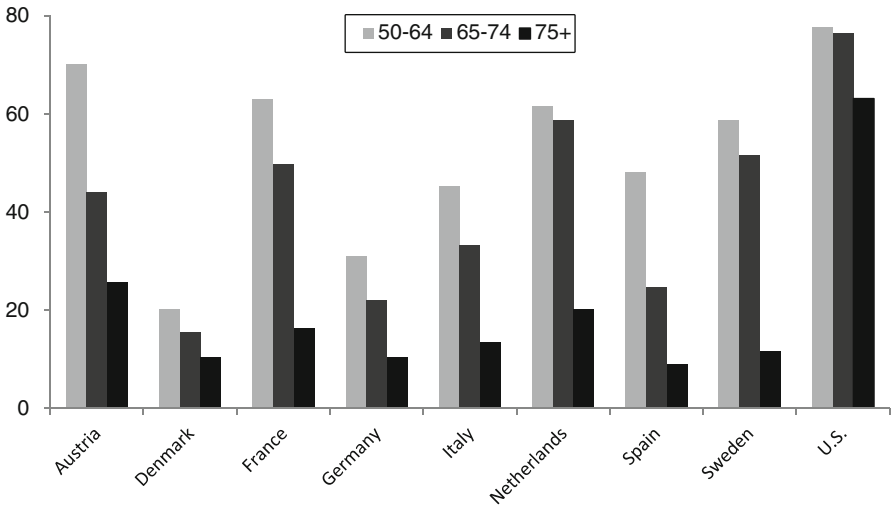

Fig. 9.1 Percentage of women who received a mammogram in previous 2 years, 2004 (Source: Howard et al. 2009; U.S. – 2004 Health and Retirement Study (HRS); Europe – 2004 Survey of Health, Ageing and Retirement in Europe (SHARE))

receiving a mammogram (63.1%), as shown in Fig. 9.1. Screening prevalence among European women aged 75 years and older ranged from 9.0% for Spain, to 25.7% for Austria. The severe drop in mammography use from ages 50–64 to 75 years and older among European women reflects age-based limits in mammography test use in many European countries.

Prostate Cancer

The serum prostate-specific antigen (PSA) test was introduced in the U.S. in the late 1980s and is the most commonly used tool for detecting prostate cancer in the U.S. Although utilization of the PSA test is widespread in the U.S., the Council of the European Union has concluded that there is insufficient evidence to recommend routine screening in Europe.

The U.S. has one of the highest percentages of men receiving a PSA test in the past year across all age groups, as shown in Fig. 9.2. Austria was the only country to have a higher prevalence of PSA test use than the U.S. among men ages 50–64 and 75 years and older, whereas the majority of European countries have a much lower screening prevalence. Austria's higher screening prevalence is likely to be attributed to prostate screening trials, such as in Tyrol, where intensive PSA screening began in 1992 (Micheli et al. 2003). Lower cancer screening prevalence in the rest of the European countries analyzed can be attributed to the European Union's strong sentiment against prostate cancer screening. Higher prevalence of test use amongst older respondents probably reflects the use of PSA as a diagnostic test as well as a screening test.

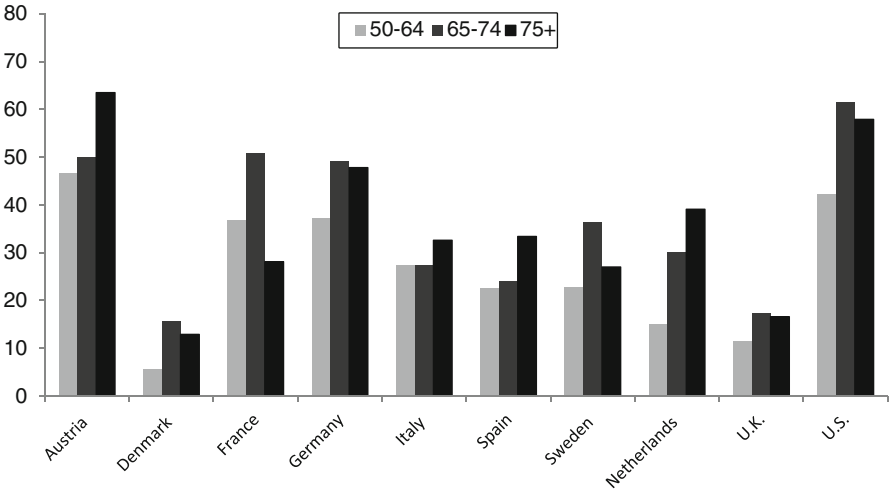

Fig. 9.2 Percentage of men who received a PSA test in previous year, 2006 (Notes: U.S. – ages 65–85, data collection year 2004; Source: Howard et al. 2009; U.S. – 2004 Medical Expenditure Panel Survey (MEPS); Europe – 2006 Eurobarometer)

Colorectal Cancer

There are marked differences in the testing modalities recommended in the U.S. and Europe. Since the mid 1990s, U.S. guidelines have recommended the use of fecal occult blood tests annually in addition to endoscopic examinations (sigmoidoscopy every 5 years or colonoscopy every 10 years) for average-risk adults aged 50 years and older. Over the last decade, colonoscopy has become the most common screening modality in the U.S. (Chen et al. 2008). Substantial increases in its use were noted after Medicare coverage was expanded in 2001 to include colonoscopy for screening purposes for average-risk individuals (Harewood and Lieberman 2004). The fecal occult blood test is the only test recommended by the Council of the European Union and is the most frequently applied method in Europe, whereas colonoscopy is seldom used as a primary screening test (Zavoral et al. 2009; Benson et al. 2007). Many European countries have been reluctant to promote endoscopic screening due to the lack of evidence from randomized trials on their efficacy in reducing colorectal cancer incidence and mortality (Atkin 2003; Pox et al. 2007).

The prevalence of colorectal cancer test use among European countries has only been reported recently (Stock et al. 2010; Stock and Brenner 2010; Howard et al. 2009). Howard and colleagues (2009) report colorectal cancer screening rates based on receipt of the FOBt or endoscopy combined for the U.S. and Europe, in which European rates, with the exception of Austria, were lower than U.S. rates across younger and older age groups. In this section, we highlight the findings by Stock and Brenner (2010), who report prevalence estimates by screening modality among adults aged 50 years and over in Europe based on the 2004 SHARE data. Prevalence

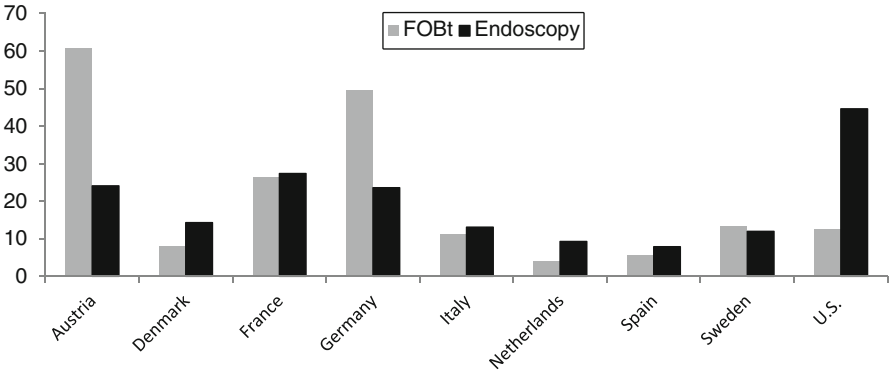

Fig. 9.3 Percentage of men aged 50+ who received a colorectal screening test in last 10 years (Notes: U.S. – FOBt within the last year; Endoscopy, sigmoidoscopy within past 5 years or colonoscopy within past 10 years; Europe – FOBt within the last 10 years; Endoscopy, sigmoidoscopy or colonoscopy within the past 10 years; Source: Stock and Brenner 2010; American Cancer Society 2009; U.S. – 2005 National Health Interview Survey (NHIS); Europe – 2004 Survey of Health, Ageing and Retirement in Europe (SHARE))

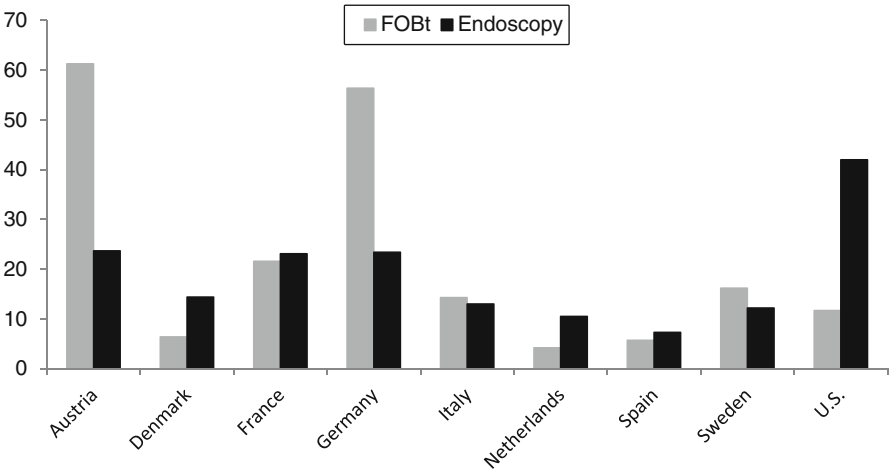

Fig. 9.4 Percentage of women aged 50+ who received a colorectal screening test in last 10 Years (Notes: U.S. – FOBt within the last year; Endoscopy, sigmoidoscopy within past 5 years or colonoscopy within past 10 years; Europe – FOBt within the last 10 years; Endoscopy, sigmoidoscopy or colonoscopy within the past 10 years; Source: Stock and Brenner 2010; American Cancer Society 2009; U.S. – 2005 National Health Interview Survey (NHIS); Europe – 2004 Survey of Health, Ageing and Retirement in Europe (SHARE))

estimates for the United States are based on 2005 NHIS data (American Cancer Society 2009).

Prevalence estimates of FOBt and endoscopy utilization among Europeans aged 50 years and older in the last 10 years were generally less than 20%, as shown in Figs. 9.3 and 9.4. Austria, France and Germany reported prevalence rates above

20% for both men and women across screening modalities. Although the Council of the European Union only recommends the FOBt for colorectal cancer screening, prevalence estimates were higher for endoscopy than for the FOBt in approximately half of the European countries analyzed. There were few significant gender differences in screening prevalence (Stock and Brenner 2010).

In the United States, endoscopy rates are higher than FOBt rates among both men and women aged 50 years and over (Meissner et al. 2006). Although recent endoscopy often includes receipt of a sigmoidoscopy in the past 5 years or colonoscopy in the last 10 years, both men and women report substantially higher prevalence of colonoscopy within the last 10 years (32.2 and 29.8%, respectively) than sigmoidoscopy within the last 5 years (7.6 and 5.9%, respectively) (Meissner et al. 2006). FOBt use in the United States is comparable to that in most European countries, however reported endoscopy use is much higher in the U.S. (Figs. 9.3 and 9.4). We assume this reflects the marked differences in the screening modalities recommended in the U.S. and Europe.

Screening and Cancer Trends

Incidence and mortality data from regional and national cancer registries allow researchers to monitor the disease among various populations and examine differences in cancer occurrence, survival, and mortality by demographic factors. Population-based cancer data have increasingly been used to evaluate the effectiveness of screening for cancers amenable to early detection and treatment on a national-level. Trends in age-standardized incidence and mortality rates from 1980 to 2005 for breast, prostate, and colorectal cancer among persons aged 50 years and older in the U.S. and several countries in Europe are provided. We examine mortality trends in two time periods, 1980–1989 and 1990–2005, to identify differences in the rate of decline in site-specific cancer deaths in relation to the use of population screening across countries.

Cancer disparities and the burden of cancer worldwide have been highlighted due to the availability of comparable regional and national-level data from Cancer Incidence in Five Continents (CI5) and the World Health Organization (WHO) Mortality Database (La Vecchia et al. 2010; Ferlay et al. 2004; Quinn and Babb 2002; Parkin et al. 2001). Cancer Incidence in Five Continents Annual Dataset (CI5*plus*) provides crude and age-standardized annual incidence based on data from national and regional cancer registries (Ferlay et al. 2010).

Incidence and mortality rates are based on the number of new or primary cancer cases and deaths occurring in a given time period in a specified population and expressed per 100,000 persons per year. To increase comparability, incidence and mortality rates are adjusted to the World standard population (Segi 1960). Anatomical sites examined include malignant neoplasms of the breast (ICD code C50), prostate (ICD code C61), and colon, rectosigmoid junction, rectum, anus, and anal canal (ICD code C18–21).

Cancer Incidence

Screening practices have had large influences on cancer diagnosis. As indicated above, screening will increase the diagnosis of more localized, curable cancers, as well as identify clinically insignificant tumors that would never be identified without screening (Bangma et al. 2007; Thompson et al. 2004). Numerous studies have shown changes in cancer incidence that parallel major changes in screening test utilization (Mettlin 2000; Glass et al. 2007; Jørgensen and Gøtzsche 2009). Marked increases in incidence are observed for particular cancers after the introduction of screening. The estimation of overdiagnosis in relation to initiation of screening is complex (Paci and Duffy 2005; Duffy et al. 2008) and varies by cancer site (Welch and Black 2010). In the U.S., overdiagnosis of prostate cancer due to PSA screening is estimated to be 15–37%, depending on race (Etzioni et al. 2002). Estimates of overdiagnosis of breast cancer based on the analysis of incidence rates before and after the implementation of breast screening programs or trials range from less than 1–33% (Paci et al. 2004, 2006; Duffy et al. 2005; Olsen et al. 2006; Zackrisson et al. 2006; Jørgensen et al. 2009), and differ by age and outcome (in situ breast vs. invasive breast cancer). We examine time trends in breast, prostate, and colorectal cancer incidence based on data from regional and national cancer registries across a number of countries. Both levels and trends in cancer incidence vary widely between the U.S. and Europe, and across Europe as well.

Breast Cancer Incidence

From 1980, there was a gradual increase in the reported incidence of breast cancer among women aged 50 years and older in the U.S. and Europe, as shown in Fig. 9.5. From 1980 to 2002, breast cancer incidence rates are higher in the U.S. compared to most European countries analyzed. Higher prevalence of mammography screening in the U.S. relative to other countries may have resulted in the higher rates of diagnosed breast cancer. The increase in incidence rates over time may reflect the progressive adoption of mammography beginning in the 1980s (Glass et al. 2007). It is also possible that some of the increase in breast cancer incidence in the United Sates up through about 2002 may have resulted from widespread use of hormone replacement therapy for potential chronic disease prevention among menopausal women beginning in the 1980s (Glass et al. 2007). The difference in oral hormone therapy use may also contribute to some of the disparities in breast cancer incidence between American and European women (Stefanick 2005).

Prostate Cancer Incidence

Since the 1990s, many European countries have experienced a gradual increase in the reported incidence of prostate cancer among men aged 50 years and older, as

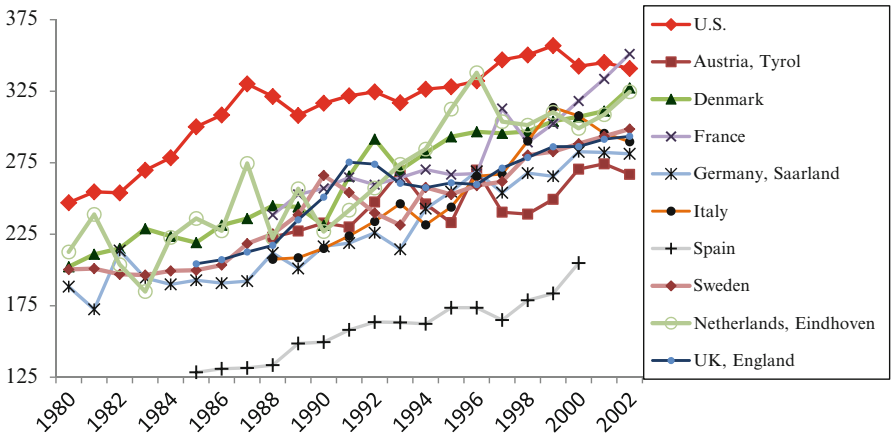

Fig. 9.5 Age-standardized breast cancer incidence among women 50+, 1980–2002 (Source: Ferlay et al. 2010)

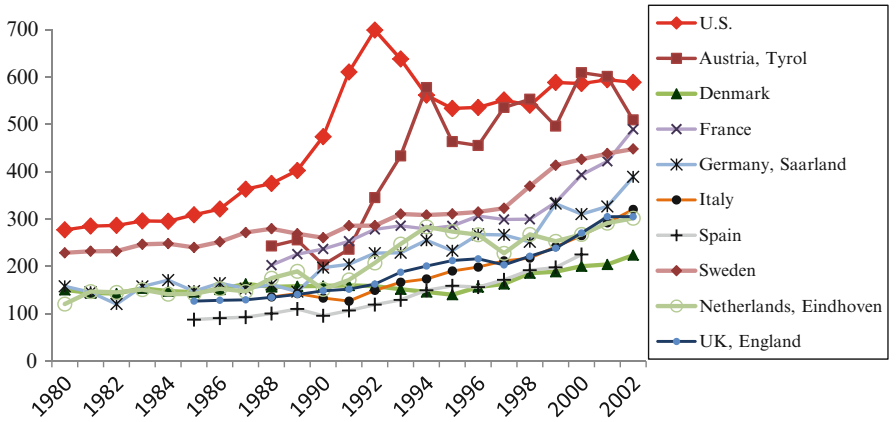

Fig. 9.6 Age-standardized prostate cancer incidence among men 50+, 1980–2002 (Source: Ferlay et al. 2010)

shown in Fig. 9.6. However, in the U.S. and Austria (Tyrol), prostate cancer incidence rates rose rapidly in the early 1990s and then declined in the late 1990s. Despite these declines, recorded prostate cancer incidence rates remained substantially higher in the U.S. and Austria compared to other European countries. This pattern parallels the introduction and widespread use of the PSA test as a screening tool in the U.S. (Quinn and Babb 2002), and the implementation of a mass prostate screening program in Tyrol, Austria (Horninger et al. 1999). The widespread implementation of prostate cancer screening has not only affected trends in prostate cancer incidence, but has also affected the features of the identified cases, such as tumor stage and grade (Rietbergen et al. 1999; Stephenson 1998).

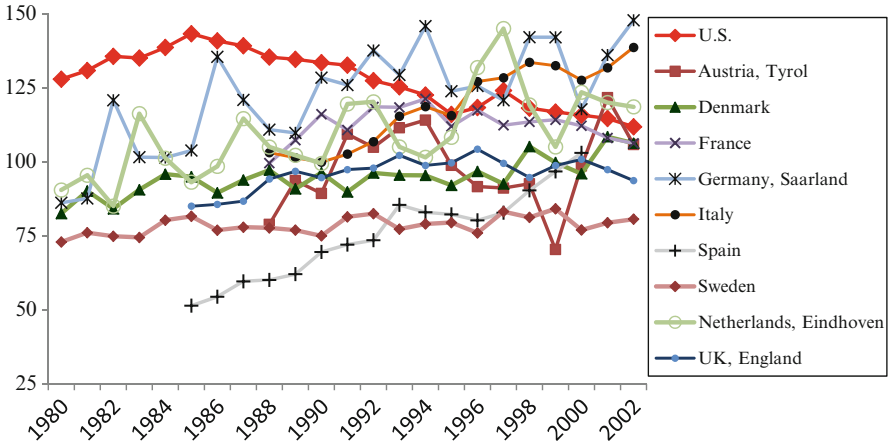

Fig. 9.7 Age-standardized colon cancer incidence among men 50+, 1980–2002 (Source: Ferlay et al. 2010)

Colon Cancer Incidence

From 1980 to 2002, reported colon cancer incidence among men and women aged 50 years and older remained stable or gradually increased in the European countries examined, whereas reported colon cancer incidence decreased among both men and women in the U.S. over this period (Fig. 9.7). It is interesting that in spite of increased screening for colorectal cancer in the U.S. (Chen et al. 2008; CDC 2011), the incidence decreased. It is possible that there have been real declines in incidence as screening prevalence has increased. One difference between screening for colorectal cancers and other cancers is that the removal of polyps that occurs with colorectal screening may reduce the incidence of cancer as well as mortality from diagnosed cancers (Rabeneck et al. 2010). Progressive adoption of colonoscopy in the U.S. is consistent with declining colon cancer incidence trends.

Cancer Survival Rates

Improved cancer survival in the U.S. and Europe is attributed to the advent of earlier diagnosis and advances in effective treatment (Wingo et al. 1998; Sant 2001; Gatta et al. 2002; Mariotto et al. 2002). Over the last 30 years, the 5-year relative survival rate for all cancers diagnosed in the U.S. has significantly increased from 50% between the years 1975 and 1977 to 68% between the years 1999 and 2005 (Horner et al. 2009). In an international comparison, the U.S. had the highest 5-year relative survival for breast, colorectal, and prostate cancer compared to the European countries included in this analysis, as shown in Table 9.1 (Coleman et al. 2008).

Table 9.1 5-year relative survival for select cancers

	Breast	Prostate	Colorectum	
	RS (%) (95% CI)	RS(%) (95% CI)	Males	Females
Austria	74.9 (71.9–78.1)	86.1 (82.9–89.4)	52.7 (48.2–57.6)	55.1 (50.8–59.7)
Denmark	73.6 (72.5–74.7)	38.4 (36.3–40.6)	44.2 (42.7–45.7)	47.7 (46.3–49.2)
France	79.8 (78.2–81.4)	73.7 (70.5–77.1)	55.6 (53.3–58.1)	61.5 (59.2–64.0)
Germany	75.5 (73.3–77.8)	76.4 (72.7–80.4)	50.1 (47.2–53.2)	55.0 (52.3–57.9)
Italy	79.5 (78.8–80.3)	65.4 (63.7–67.2)	50.7 (49.7–51.8)	52.7 (51.7–53.8)
Spain	77.7 (76.4–79.0)	60.5 (57.6–63.6)	52.5 (51.0–54.1)	54.7 (53.1–56.4)
Sweden	82.0 (81.2–82.7)	66.0 (64.7–67.3)	52.8 (51.6–54.1)	56.2 (55.0–57.4)
Netherlands	77.6 (76.6–78.6)	69.5 (67.2–71.9)	53.6 (51.5–55.7)	55.1 (53.3–57.0)
U.K.	69.7 (69.4–70.1)	51.1 (50.4–51.8)	42.3 (41.8–42.8)	44.7 (44.3–45.2)
U.S.	83.9 (83.7–84.1)	91.9 (91.7–92.1)	59.1 (58.8–59.5)	60.2 (59.8–60.5)

Source: Coleman et al. (2008), data for selected countries taken from Table 9.2
Notes: Age-standardized to ICSS weights; Survival estimates based on adults (aged 15–99 years) diagnosed with cancer during 1990–1994 and followed up to 1999

The links between differences in survival rates and changes is survival rates over time, however, must be interpreted with caution due to the effects of screening activities (Farrow et al. 1996). By detecting tumors and precancerous lesions before symptoms are present, the disease may be more treatable and have a better prognosis. However, screening may also lead to the detection of both benign and pre-malignant tumors that will never become symptomatic or progress further. Second, there may also be cases where earlier detection of the disease through screening has no effect on disease outcome, but leads to an artificial increase in individual survival time from diagnosis to death simply as a result of an earlier diagnosis. Slower-growing tumors have a greater likelihood of being detected at preclinical stages by periodic screening, leading to a length bias in survival rates (Walter and Stitt 1987; Prorok et al. 1990). It is probable that higher or improved survival rates result from greater detection of latent, slow-growing tumors that are already associated with a greater likelihood of survival rather than reductions in mortality from tumors of the same size and lethality as those identified before screening. In many respects, trends in cancer mortality may provide a better indication of the effectiveness of cancer control measures than trends in cancer incidence or cancer survival rates.

Cancer Mortality

The examination of population-based cancer mortality trends and retrospective analyses of screening prevalence have been used to infer the extent of the possible public health benefit of population-based screening. In the past two decades, declines in breast, prostate and colorectal cancer mortality have been observed in the U.S. and Europe (Preston and Ho 2010; Rohde et al. 2009; Karim-Kos et al. 2008; Collin et al. 2008; Coleman et al. 2008; Bouchardy et al. 2008; Verdecchia

Table 9.2 Change in breast cancer incidence and mortality, and screening among women ages 50+

	Incidence change (%)		Mortality change (%)			Mammography in past 2 years (%)
	Annual		Annual		Overall	Ages 50–64
	1980–1989	1990–2002	1980–1989	1990–2005	1980–2005	2004
Austria		1.0*	1.6*	−1.4*	−8.6	70.0
Denmark	2.1*	2.1*	0.7*	−1.0*	−12.5	20.2
France		2.5*	0.5*	−0.7*	−2.5	63.0
Germany	2.2*	2.2*	0.8*	−1.0*	−3.2	30.9
Italy		2.6*	1.1*	−1.4*	−5.5	45.2
Spain		2.3*	2.9*	−1.4*	3.9	48.1
Sweden	2.3*	1.3*	−0.8*	−0.8*	−17.2	58.7
Netherlands	2.2*	2.2*	0.3	−1.7*	−20.1	61.6
U.K.		1.0*	0.6*	−2.5*	−26.8	NA
U.S.	3.2*	0.5	0.4*	−2.2*	−26.1	77.7

Source: Ferlay et al. (2010); WHO Mortality Database [http://www.encr.com.fr]; Screening data: Howard et al. (2009); U.S. – 2004 Health and Retirement Study (HRS); Europe – 2004 Survey of Health, Ageing and Retirement in Europe (SHARE)
Notes: Incidence estimates based on regional data for the following countries: Austria (Tyrol), Germany (Saarland), The Netherlands (Eindhoven), United Kingdom (England)
*AAPC is statistically significant (two-sided $p<0.05$)
NA: Not Available

et al. 2007; Ward et al. 2006; Boyle and Ferlay 2005a; Levi et al. 2005; Baade et al. 2004; Tyczynski et al. 2004; Hsing et al. 2000; Pito et al. 2000). Recent declines in cancer-specific mortality in countries with high uptakes of screening tests may be interpreted as some evidence of the effectiveness of screening, however ecological analyses should be interpreted with caution. There are numerous other factors that can affect mortality, including treatment. There is also a lag time between when a cancer is identified and when a death is prevented, making it difficult to relate screening to cancer mortality trends.

The rate of decline in age-standardized breast, prostate, and colorectal cancer mortality rates among persons aged 50 years and older in the U.S. and several countries in Europe are examined below. Joinpoint regression (Joinpoint Version 3.3; National Cancer Institute, Bethesda, MD 2008) is used to estimate average annual percent change (AAPC) to summarize the mortality trend over the intervals 1980–1989 and 1990–2005.

Breast Cancer

From 1980 to 1989, significant increases in breast cancer mortality rates are observed in most countries except for Sweden, where a significant decrease in mortality is observed (Table 9.2). After rising mortality rates throughout the 1980s, significant declines in breast cancer mortality rates are observed in all countries from 1990 to 2005 (Fig. 9.8). In this time period, breast cancer mortality rates

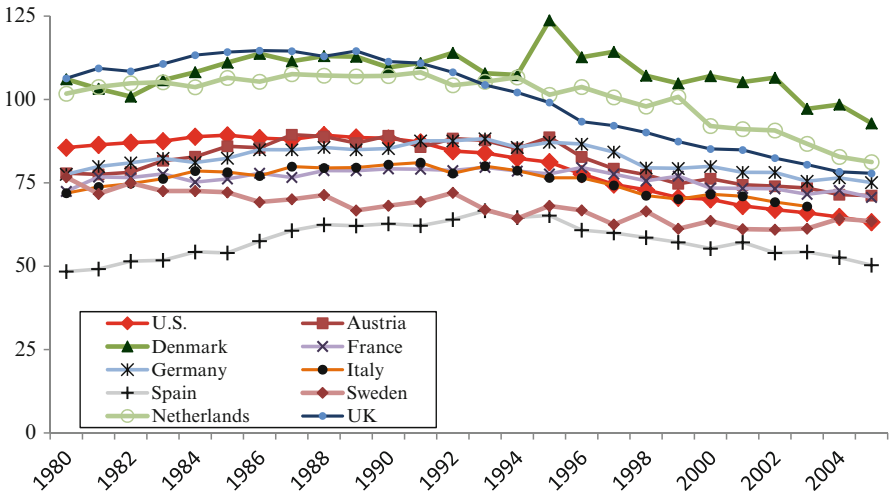

Fig. 9.8 Breast cancer mortality among women 50+, 1980–2005 (Source: WHO Mortality Database [http://www.encr.com.fr])

decreased by an average annual percentage of −0.7 to −2.5% per year, as shown in Table 9.2. The U.S. and U.K. experienced the fastest rates of decline from 1990 to 2005, −2.2 and −2.5% per year, respectively, and experienced the highest overall decline in age-standardized breast cancer deaths of approximately 26% from 1980 to 2005.

The United States and U.K., which experienced the fastest rates of decline and the highest overall decline in breast cancer mortality, have the highest screening prevalence among the group of countries analyzed here. Although self-reported data on current mammography use were not available for the U.K., screening prevalence for mammography among women aged 50–70 years old in 2006/2007 is estimated to be approximately 74% (Patnick 2009). However, from 1990 to 2005, countries with low screening prevalence, such as Denmark and Germany, experienced rates of decline in breast cancer mortality similar to rates experienced by countries with a much higher screening prevalence, such as France. This finding would seem to indicate that screening has played some role in the declines in breast cancer but that other factors, such as improved treatment using adjuvant multiagent chemotherapy and tamoxifen, may have also been important (Mariotto et al. 2002; Harlan et al. 2002).

Prostate Cancer

Between 1980 and 1989, significant increases in prostate cancer mortality rates are observed for all countries except Sweden (Table 9.3). After rising mortality rates from prostate cancer occur throughout the 1980s, significant declines in mortality rates are observed in most countries from 1990 to 2005, as shown in Fig. 9.9. In this period, mortality rates decreased by an average annual change of –0.9 to –3.2% per

Table 9.3 Change in prostate cancer incidence and mortality, and screening among men ages 50+

	Incidence change (%)		Mortality change (%)			PSA test in past year (%)
	Annual		Annual		Overall	Ages 50–64
	1980–1989	1990–2002	1980–1989	1990–2005	1980–2005	2006
Austria		8.8*	1.6*	−1.7*	−14.6	46.5
Denmark	1.0*	2.9*	1.5*	0.3	14.5	33.8
France		6.1*	1.2*	−1.9*	−17.4	36.8
Germany	4.6*	4.6*	1.4*	−1.5*	−7.4	37.2
Italy		8.4*	0.5*	−1.0*	−3.6	27.3
Spain		8.3*	0.6*	−1.1*	−13.2	22.6
Sweden	2.2*	4.4*	0.2	0.1	1.4	22.8
Netherlands	2.5*	4.9	1.4*	−1.2*	−4.5	15.0
U.K.		6.1*	3.2*	−0.9*	17.0	11.5[a]
U.S.	5.0*	1.6	1.0*	−3.2*	−30.4	42.2[b]

Source: Ferlay et al. (2010); WHO Mortality Database [http://www.encr.com.fr]; Screening data: Howard et al. (2009); U.S. – 2004 Medical Expenditure Panel Survey (MEPS); Europe – 2006 Eurobarometer

Notes: Incidence estimates based on regional data for the following countries: Austria (Tyrol), Germany (Saarland), The Netherlands (Eindhoven), United Kingdom (England)

*AAPC is statistically significant (two-sided $p<0.05$)

[a]Data for Great Britain

[b]2004 data

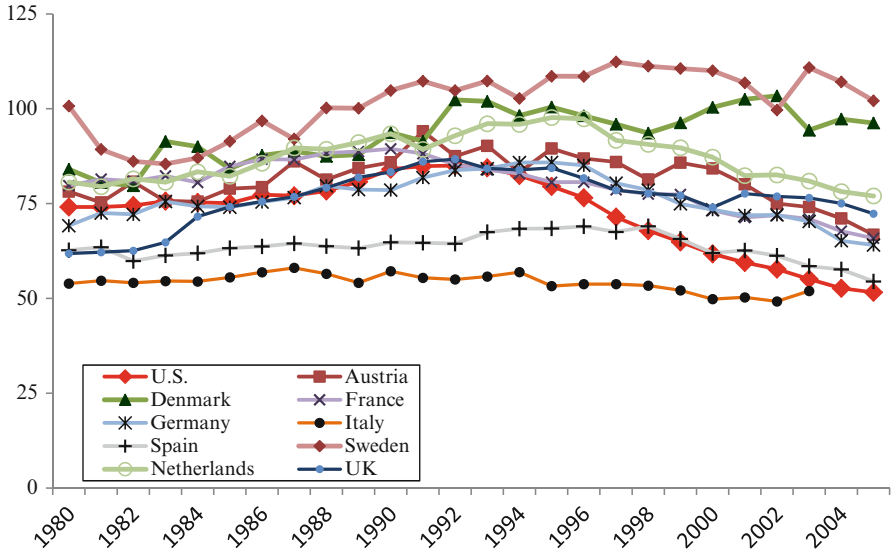

Fig. 9.9 Prostate cancer mortality among men 50+, 1980–2005 (Source: WHO Mortality Database [http://www.encr.com.fr])

year among men aged 50 years and older (Table 9.3). The U.S. experienced the fastest rate of decline of −3.2% per year from 1990 to 2005 and the highest mortality reduction in age-standardized prostate cancer rates from 1980 to 2005, 30.4%.

Countries with the highest screening prevalence, such as the U.S., Austria, France, and Germany, experienced the fastest rates of decline in prostate cancer mortality among men aged 50 years and older from 1990 to 2005 and the greatest overall mortality change from 1980 to 2005. In contrast, countries with the lowest screening prevalence, such as Denmark and the U.K., have experienced little or no decline in prostate cancer mortality from 1990 to 2005 and have actually experienced an increase in overall prostate cancer mortality from 1980 to 2005. Thus, these data suggest that national trends in prostate cancer mortality have been significantly affected by the use of screening.

Colorectal Cancer

From 1980 to 1989, some countries experienced significant increases in colorectal cancer mortality, while other countries experienced stable or small declines in mortality among men (Table 9.4). In this time period, most countries, however, experienced significant declines in colorectal cancer among women. American men and women experienced the fastest decline in mortality from 1980 to 1989, −1.0 and −1.3% per year, respectively. From 1990 to 2005, most countries experienced declines in colorectal cancer mortality among both men and women (Figs. 9.10 and 9.11). American men and women continued to experience one of the fastest mortality declines, of −2.4 and −2.5% per year, throughout this period, and experienced the highest overall decline in age-standardized colorectal cancer deaths between 1980 and 2005, 37.6% and 41.0%, respectively (Table 9.4). The U.K. and Austria experienced the fastest decline in colorectal cancer mortality −2.7% per year among women. Spain and Italy were the only countries to experience a rise in colorectal cancer mortality rates from 1980 to 2005, especially among men. From 1980 to 2005, mortality rates among Spanish women increased by 33%, while rates increased by an alarming 95% among Spanish men.

Similar to patterns seen for breast and prostate cancer, countries with higher colorectal cancer screening prevalence, such as the U.S., Austria, and Germany, experienced faster rates of decline in colorectal cancer mortality, while countries with extremely low screening prevalence, such as Italy and Spain, experienced little or no decline in colorectal cancer mortality.

Issues and Challenges

The reduction in cancer death rates over the past two decades in the U.S. and other high-income European countries appears to be a persuasive argument in support of screening and early detection. Issues surrounding over diagnosis and over treatment

Table 9.4 Change in colorectal cancer incidence and mortality, and screening among 50+, by sex

	Colon cancer incidence change (%)		Rectum and anus cancer incidence change (%)		Colorectal cancer mortality change (%)			Colorectal cancer tests in past 10 years (%); Ages 50+	
	Annual		Annual		Annual		Overall	Endoscopy	FOBT
	1980–1989	1990–2002	1980–1989	1990–2002	1980–1989	1990–2005	1980–2005	2004	2004
Males									
Austria		−0.3		1.5	0.5*	−1.9*	−26.6	24.1	60.7
Denmark	0.7*	0.7*	−0.1	−0.1	−0.1	−1.2*	−13.3	14.3	8.1
France		−0.8*		−0.9*	−0.4*	−1.3*	−22.1	27.4	26.3
Germany	1.7*	1.7*	−2.7	1.6*	0.4*	−1.4*	−19.2	23.6	49.7
Italy		3.0*		0.6	0.8*	−0.1	6.7	13.1	11.3
Spain		3.5*		1.9*	4.2*	1.9*	94.8	7.9	5.6
Sweden	0.3*	0.3*	0.3*	0.3*	−0.6*	−0.6*	−18.2	12.0	13.3
Netherlands	1.3*	1.3*	1.0*	1.0*	−0.4*	−0.4*	−11.7	9.3	4.0
U.K.		−0.1		0.2	0.3	−2.2*	−25.6		
U.S.	0.5	−1.4*	−0.4	−1.4	−1.0*	−2.4*	−37.6	[1]44.6	[1]12.7
Females									
Austria		−1.3		1.1	−1.0*	−2.7*	−39.3	23.7	61.3
Denmark	−0.3	−0.3	0	0	−0.9*	−0.9*	−25.0	14.4	6.4
France		−0.7*		−0.6	−1.2*	−1.2*	−24.6	23.1	21.6
Germany	4.2*	0.2	−2.7	1.2*	−0.5*	−2.5*	−36.2	23.4	56.4
Italy		1.5*		−0.4	0.9	−0.6*	−0.2	13.0	14.3
Spain		2.4*		0.2	3.5*	0.2	33.2	7.3	5.7
Sweden	0	0	0	0	−1*	−1*	−24.2	12.2	16.2
Netherlands	0.8*	0.8*	0.5	0.5	−1.1*	−1.1*	−20.1	10.5	4.2
U.K.		−1.2*		0.3	−1.1	−2.7*	−41.1		
U.S.	−1.0*	−1.0*	−1.2*	−1.2*	−1.3*	−2.5*	−41.0	[a]42.0	[a]11.7

Source: Ferlay et al. (2010); WHO Mortality Database [http://www.encr.com.fr]; Screening data: Europe – 2004 Survey of Health, Ageing and Retirement in Europe (SHARE); Stock and Brenner (2010); U.S. – 2005 National Health Interview Survey (NHIS); American Cancer Society (2009)
Notes: Incidence estimates based on regional data for the following countries: Austria (Tyrol), Germany (Saarland), The Netherlands (Eindhoven), United Kingdom (England)
*AAPC is statistically significant (two-sided $p<0.05$)
[a]2005 data for colorectal cancer tests

remain at the forefront of developing policies for population screening (Elmore et al. 2005; Welch 2009; Jørgensen and Gøtzsche 2009; Esserman et al 2009). Greater emphasis is now placed on quantifying the overall risk-benefit profile of a screening modality in order to determine its value for population screening.

In addition, it is hard to separate the effect of screening from other factors including improved diagnosis through technological advances and development and implementation of more effective therapy (Etzioni et al. 1999; Mariotto et al. 2002; Meng et al. 2002). The recent declines in site-specific cancer mortality can only be attributed to screening if screening is followed by appropriate diagnoses, effective

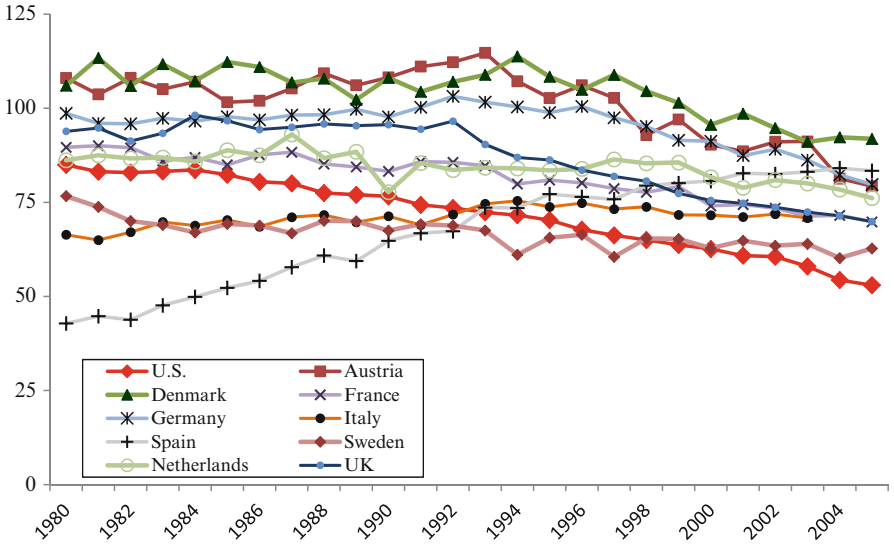

Fig. 9.10 Colorectal cancer mortality among men 50+, 1980–2005 (Source: WHO Mortality Database [http://www.encr.com.fr])

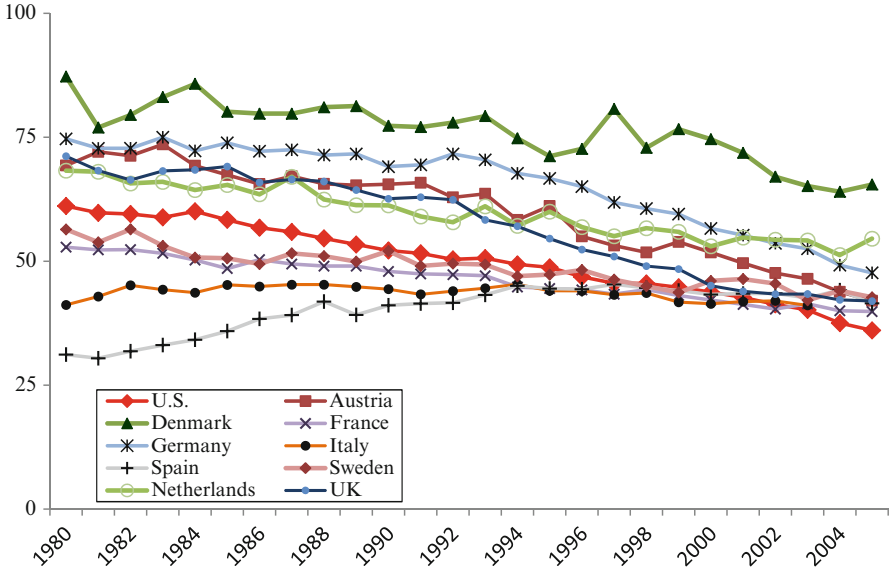

Fig. 9.11 Colorectal cancer mortality among women 50+, 1980–2005 (Source: WHO Mortality Database [http://www.encr.com.fr])

treatment, and follow-up care. The unique impact of screening on cancer mortality is difficult to establish because advances in treatment known to alter disease prognosis occurred concurrently with the widespread use of screening modalities. For example, the advent of nerve-sparing surgical techniques in the early 1980s,

followed by innovations in radiotherapy and hormonal treatment, led to curative treatment options, often multimodal, for patients diagnosed with varying stages of cancers in the prostate and breast (Etzioni and Feuer 2008; Nelson et al. 2009).

Treatment patterns and access to cancer care also differ markedly across countries. Vast inequalities in resources for cancer care are reported in Europe including the number of medical oncology facilities and specialists in each country (ESMO 2006). For example, higher numbers of medical oncology facilities per million of the population are reported in Northern Europe than in the Mediterranean countries (ESMO 2006). National and regional variations in the provision of radiotherapy have also been documented (Bentzen et al. 2005). The consequence of inadequate access to radiotherapy is increased waiting times for treatment, which is likely to have detrimental effects on treatment outcomes (Rutqvist 2006).

The quality and availability of cancer prevention and treatment modalities and resulting cancer survival have been linked to macro-economic determinants, such as gross domestic product (GDP), the total public expenditure on health (TPEH), and total national expenditure on health (TNEH) (Micheli et al. 2003). European countries with high TNEH tended to have high cancer survival rates compared to countries with low TNEH. Based on this analysis, it is not surprising that cancer survival rates are among the highest in the U.S., which has the highest total health expenditure among all high-income countries (OECD 2006).

Conclusion

Countries with the highest screening prevalence have generally experienced faster declines in mortality from 1990 to 2005, while countries with lower screening prevalence have experienced increases or little change in cancer mortality in this period. The results in this study reveal that despite higher reported incidence rates for most cancers analyzed, Americans currently have among the lowest breast, prostate, and colorectal cancer mortality rates and experienced some of the fastest declines in breast, prostate, and colorectal cancer mortality rates from 1990 to 2005, compared to their European counterparts. However, this was not the case in the 1980s.

The reduction of cancer death rates over the past two decades in the U.S. and other high-income European countries among persons aged 50 years and older appears to be a persuasive argument in support of screening and early detection. The complexity of the relationship between mortality trends and screening prevalence lies within the countries in the middle. Some countries with moderate prevalence of screening have experienced significant declines in cancer-specific mortality rates comparable to those with the highest prevalence of screening.

The comparison of cancer incidence and mortality rates between regions or countries with different screening uptakes plays an important role in the current debate on the value of population screening (Etzioni and Feuer 2008; Mettlin 2000). Despite their limitations, ecological or geographical studies are useful for monitoring the effectiveness of population interventions, such as screening initiatives and programs. In the absence of conclusive findings from randomized trials, these studies

help generate hypotheses about the public health benefit of cancer screening and highlight disparities in the burden of cancer across populations. Continued monitoring of incidence and mortality trends, along with prevention and treatment practices, may increase our understanding of the relationship between screening and mortality reduction.

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