Global incidence and mortality of prostate cancer: analysis of temporal patterns and trends in 36 countries

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Abstract

Background

Prostate cancer (PCa) is one of the leading causes of mortality and morbidity globally, but its specific geographical patterns and temporal trends are under-researched.

Objective

To test the hypotheses that the incidence of PCa was higher and its mortality was lower in countries with higher socioeconomic development, and that the temporal trends of incidence increased whilst mortality decreased with time.

Design, Settings and Participants

Data on age-standardized incidence/mortality rates in 2012 were retrieved from the GLOBOCAN database. Temporal patterns were assessed for 36 countries obtained from the Cancer Incidence in Five Continents volumes I-X and the WHO mortality database. The correlation between the incidence/mortality rates and socioeconomic indicators (Human Development Index [HDI] and Gross Domestic Product [GDP]) was evaluated.

Outcome Measurements and Statistical Analysis

The average annual percent change of PCa incidence and mortality in the most recent 10 years from join-point regression.

Results and Limitations

Reported incidence rates of PCa varied more than 25-fold worldwide in 2012, with the highest incidence rates observed in Micronesia/Polynesia, the US and the European countries. The

mortality rates paralleled the incidence rates except for Africa, where the mortality rates were the highest. Countries with higher HDI (r=0.58) and GDP per capita (r=0.62) reported greater incidence rates. Based on figures in the recent 10 years, most countries experienced increases in incidence, with sharp rise in incidence rates in Asia, Northern and Western Europe. A substantial reduction in mortality rates was reported in most countries, except in some Asian countries and Eastern Europe where mortality increased. Figures in regional registries could be underestimated.

Conclusions

The incidence of PCa increased whilst its mortality decreased in most countries. In countries with higher socioeconomic development, the reported incidence was higher.

Patient Summary

The PCa incidence had high variation geographically and over time with smaller variations in mortality.

Introduction

Prostate cancer (PCa) is the second commonest diagnosed malignancy and the fifth leading cause of cancer mortality in men, accounting for a substantial public health burden [1]. Currently, the established risk factors for PCa include advanced age, black race, a family history of the disease, and certain genetic polymorphisms [2]. There is a strong prospect to reduce PCa induced mortality by screening [3, 4]. Hence, it is crucial to understand its global epidemiological trends.

Previous studies describing its international trends were based on figures from registries in early 2000s [5-7], did not take into account the socioeconomic development of each country when comparisons were made [8, 9], or depended on model-based clustering [10]. Analyzing the patterns and temporal trends of PCa could quantify geographical variation, identify high-risk populations and delineate the extent of PSA testing uptake [9]. These epidemiological data could also be linked to the future prospects of cancer prevention for policy-makers [11].

A survey based on the UK regional cancer registry found that a substantial socioeconomic gradient exists in the use of radiotherapy or surgery in men diagnosed with prostate cancer, as well as the application of screening tests for PCa [12]. The study calls for further correlations of the incidence and mortality patterns in countries with various degrees of socioeconomic development. Therefore, we tested the hypothesis that the incidence and mortality of PCa was associated with higher and lower levels of socioeconomic development and productivity, respectively, across different countries. In addition, a recent study [13] pinpointed a substantial increase in incidence but decrease in mortality of PCa in the US. However, it is unknown

whether similar trends might exist in other countries, and evaluation of its global incidence and mortality figures is one of the important research perspectives. Therefore, we sought to test the hypothesis that its global incidence showed an increasing trend and its mortality decreased in most countries.

Materials and Methods

Source of Data

The incidence and mortality estimates for PCa (ICD-10 C61) were retrieved from the GLOBOCAN database for 184 countries in 2012 [1]. We made reference to a recent epidemiological study on colorectal cancer and used similar methodology [11]. We obtained data on the Human Development Index (HDI) and Gross Domestic Product (GPD) for each country in 2012 from the United Nations Human Development Report [14], which highlights the progress on human development over the past quarter century by reporting the different statistical indexes. HDI is a composite index of life expectancy, education period, and income per capita indicators [14]. We extracted the incidence and mortality figures from GLOBOCAN (2012) for the various continents (**Table 1**), and plotted the age-standardized incidence and mortality against HDI and GDP per capita of the same calendar year (**Figures 1a and 1b**). For temporal trend analysis, we extracted incidence data for the high quality national population-based cancer registries from the Cancer Incidence in Five Continents (CI5) series Volumes I-X [15], as well as the WHO mortality database for mortality data for all 36 countries (**Figure 2**). There were 11 countries for which more comprehensive, updated data were available (as compared with CI5), and hence were used to replace the data from CI5 (for incidence) and the WHO mortality database (for mortality). These include the US [16], New Zealand [17], Australia [18], the European Cancer Observatory [19], and the Nordic Cancer Registries [20].

The incidence data were allocated into different categories according to the International Classification of Diseases 10^{th} revision (ICD-10, C61), whereas mortality data were categorized based on the ICD 9^{th} (185) up to 1991 and 10^{th} version (C61) thereafter. More developed regions refer to all regions of Europe, Northern America, Australia/New Zealand and Japan. Less

developed regions include all regions of Africa, Asia (excluding Japan), Latin America and the Caribbean, Melanesia, Micronesia and Polynesia [1].

For mortality data, we made reference to the WHO mortality data series where data quality attained criteria of medium level or above [21], representing data with extensive coverage, high accuracy and completeness. Death certificates acted as the primary data source, and were compiled by the International Agency for Research on Cancer (IARC). We adopted age-standardized rate (ASR) using the world standard population [22].

Statistical Analysis

We employed joinpoint regression analysis to examine the incidence and mortality trends [23]. This technique fits a series of joined straight lines to the trend of ASR [23]. Logarithmic transformation of the rates was performed with computation of the standard errors based on binomial approximation. We specified a maximum number of three joinpoints as analysis options. To determine the direction and magnitude of the recent trends, the average annual percentage change (AAPC) and the respective 95% confidence intervals (C.I.) were evaluated for the last available 10 years. The AAPC was calculated as a geometrically weighted average of the various APCs from the joinpoint regression analysis by the joinpoint trend analysis software, with weights being equivalent to the length of each segment during the specified time interval [24]. We reported all data for the incidence and mortality trends in all countries where data were available. However, the most recent 10 years was chosen as the timeframe for evaluating temporal trend changes, as was considered a more commonly used time period adopted in previous publications on global epidemiology of colorectal cancer [13] and breast cancer [25]. In

describing the temporal trends, the terms increase or decrease was used based on the statistical significance of AAPC when compared to zero. Any AAPC with 95% C.Is overlapping with zero was considered stable, based on the same definition adopted by previous similar studies [13, 25].

The ASRs were plotted against the HDI and GDP per capita, respectively. The HDI was divided into four distinct categories, including low (≤0.534), medium (0.534-0.710), high (0.710-0.796) and very high (>0.796) [14]. Simple linear regression and correlation coefficients were employed to examine their associations. We also assessed whether non-linear associations had better goodness-of-fit. All p values<0.05 were regarded as statistically significant.

Results

Incidence and mortality of prostate cancer in 2012

A total of 1.11 million new cases of PCa and 307,500 PCa-related deaths were reported in 2012 (**Table 1**). The incidence rates of PCa varied more than 25-fold worldwide in 2012 [1]. The highest were found in Australia/New Zealand (ASR 111.6 per 100,000), North America (97.2) and Western Europe (94.4), and the lowest were reported in South-Central Asia (4.5) (**Table 1**). Southern Africa (61.8), Western Asia (28.0), North America (97.2), Western Europe (94.4), and Australia/New Zealand (111.6) were regions where the incidence figures were the most prominent when compared with other world regions in the same continent. When compared with the incidence figures estimated in 2008 [10], a sharp rise was observed in Western Asia (28.0 in 2012 vs. 13.8 in 2008).

PCa mortality rates varied more than 10-fold worldwide in 2012. Despite the much higher incidence in more developed than less developed regions (69.5 vs. 14.5), the difference in mortality figures was comparatively modest (10.0 vs. 6.6). The highest death rates were reported in the Caribbean (29.3). The lowest estimated mortality rates were found for most regions of Asia (3.8) and Northern Africa (7.0).

Correlation between incidence/mortality and socioeconomic development

Figure 1a shows the correlation between PCa incidence/mortality and HDI based on simple linear regression analysis. The ASR of incidence increased with higher levels of HDI ($r=0.58$, $p<0.001$), whilst the ASR of mortality did not correlate with HDI ($r=0.09$, $p=0.2$). Similarly,

higher incidence was associated with increasing GDP per capita ($r=0.62$, $p<0.001$) but there was no significant correlation between mortality and GDP per capita ($r=0.11$, $p=0.2$) (**Figure 1b**). The significant associations between the ASR figures and HDI presented the best goodness-of-fit when tested for linear relationship.

Incidence and mortality trends

There were 23 countries with increasing incidence trends, 3 countries with decreasing incidence, and 10 countries with stable incidence. There were 5 countries with increasing mortality, 22 countries with decreasing mortality, and 11 countries with stable mortality trends. We identified six groups of countries based on their temporal characteristics of incidence and mortality (**Table 2; Figure 2; Suppl Figure 1**). These included the below categories:

Group A: increasing incidence and increasing mortality

There were only three countries that reported increase in both incidence and mortality rates (**Figures 3 and 4**). The Philippines, the only country with medium HDI included in this study, encountered a drastic rise in incidence (AAPC=4.5, 95% C.I. 2.8, 6.3) and mortality (AAPC=11.4, 95% C.I. 9, 13.9).

Group B: increasing incidence and decreasing mortality

All countries in this group had very high HDI except Brazil. Among them, the highest incidence was observed in Brazil (AACP=11.9, 95% C.I. 6.9, 17) and Japan (AAPC=8.8, 95% C.I. 5.9, 11.8). The reduction in mortality was most marked in France (AAPC=-3.9, 95% C.I. -4.2, -3.6).

Group C: increasing incidence and stable mortality

Lithuania (AAPC=21.4, 95% C.I. 16.1, 26.9) reported a very substantial increase in incidence, followed by Estonia (AAPC=11.1, 95% C.I. 8.4, 13.9).

Group D: stable incidence and decreasing mortality

Most were countries with very high HDI; Canada (AAPC=-3.4, 95% C.I. -3.9, -2.9) and Austria (AAPC=-3.1, 95% C.I. -3.8, -2.5) experienced the largest decline in mortality rates.

Group E: stable incidence and stable mortality

Three countries has stable trends for both incidence and mortality. These included Costa Rica, Iceland, and Malta, with the first nation having high HDI.

Group F: decreasing incidence and decreasing mortality

Three countries that had very high HDI, namely Finland, Sweden and the United States, were included in this category. The reduction in incidence and mortality was modest.

Discussion

This study presented a comprehensive epidemiological analysis of the global profiles of PCa incidence and mortality based on high quality data. As of 2012, the Oceania, America and the European countries followed by Africa suffered from the highest incidence, whilst Asia was the least affected continent except Western Asia. The mortality rates paralleled that of the incidence figures except Africa, where the mortality rate was the highest. Countries with higher levels of human development and GDP per capita reported greater incidence but not mortality rates. The correlation coefficients of HDI (0.57) and GPD (0.62) for the incidence of PCa were high. Taking into account the average change of incidence in the previous 10 years, a total of 24 and 5 (out of 36) countries, respectively, experienced increases in incidence and mortality rates. There were sharp rises in incidence rates in Europe, Asia and less developed countries in Latin America and the Caribbean. Substantially lower mortality rates were observed for the majority of the countries with time, including Europe, and Northern America.

Several reasons could explain the wide geographical variations in PCa incidence and its temporal trends. Prostate screening, diagnostic ascertainment, and population risk factors have been attributed as potentially influential factors [11]. An increasing application of transurethral resection of the prostate and the use of prostate specific antigen (PSA) has likely been affecting the observed incidence of PCa in many more developed countries [11, 27]. In 1986, the US Food and Drug Administration has approved its use to monitor disease progression, and late in 1994 endorsed its application for prostate cancer screening among men aged 50 years or above [28]. Other possible influencers of the incidence figures include genetic, lifestyle, and environmental

factors, but none of them could cause an extremely rapid rise in incidence as observed in most countries, except prostate screening. A notable finding consists of the higher incidence of PCa in Africa, the Caribbean and Brazil, where the majority of the populations consists of Black and Mulatto individuals. This might be explained by the modulation of PCa risk via genetic disposition [30]. Major reasons for the declining mortality trends may include advances in treatment options for PCa, including radical prostatectomy, hormonal therapy and radiation therapy [10]. With the more extensive use of PSA to screen for the disease, more early stage malignancy could be identified and managed in a timely manner. Nevertheless, some nations such as the Philippines, the Russian Federation, and Belarus reported significantly increasing mortality rates. In particular, the mortality rates in Africa were very high. These figures might reflect limited healthcare services and accessibility to early screening and treatment. Another notable finding which requires future studies includes that countries with high HDI and GDP per capita were associated with higher incidence, but not with lower mortality of PCa despite better technology with more screening initiatives. There is a chance that not all countries with high HDI or GDP may have implemented screening programmes for long enough to allow mortality reduction to be realized, or that the uptake rate may not have been optimal. In addition, one of the possible explanations could be attribution bias due to potentially different healthcare systems for recording the causes of incidence and mortality.

This study presented and analyzed the most up-to-date epidemiological data on PCa, yet some limitations should be addressed. Firstly, failure or under-reporting of PCa diagnosis could lead to bias in cancer registration especially in relatively less-developed nations [26]. Figures in regional cancer registries could be underestimated owing to limited local facilities, and the precision of

data in these local/regional data is generally lower than that of national data. On the contrary, in countries where estimates were based on a single cancer registry in more urbanized, resource privileged areas, the presented figures could be overestimated if the countries consist of extensive rural populations. In addition, only one-third and one-fifth of the world's countries, respectively, reported incidence and mortality data of high quality. The quality of mortality data in terms of coverage, accuracy, and completeness varies substantially from country to country [29]. Also, the analysis of relationship between socioeconomic measures and the epidemiological figures could be confounded by detection and attribution biases, such as that introduced by the inaccuracy of death certificates and differences in case ascertainment or reporting mechanisms across different countries. Hence, one might not conclude that there exists a definite correlation between the incidence/mortality figures and the country-specific socioeconomic development; rather, the analysis presented a preliminary finding where countries with higher HDI/GDP were found to have higher PCa incidence. Lastly, despite our best efforts to analyze the most recent figures, the data used are from 2012 at the latest and the most contemporary situations will need further updates.

Conclusion

The incidence rates of PCa increased in most countries examined in this study, and the mortality rates declined in most countries, especially in more developed nations. With population ageing and population growth, clinicians and policy-makers might expect a further substantial rise in incidence trends not only attributable to ageing population alone. The absolute incidence of PCa will continue to increase much more than the curves in this paper imply. Even in countries with

stable age-standardised incidence and mortality, the number of men diagnosed with and dying of prostate cancer will substantially increase. Hence, more healthcare resources are needed to cope with the treatment of patients diagnosed with PCa, in particular for the more resource-deprived countries. Future studies should explore the underlying reasons for these epidemiological trends as well as the associations between the incidence/mortality figures and other socioeconomic measures.

Author Contributions

MCSW, BWG, HHXW, JJYS conceived the study. All authors contributed to the study design. MCSW and FDHF retrieved the data and composed the graphs. BWG provided statistical advice. FDHF and CL conducted the statistical analysis. MCSW and HHXW wrote the first draft of the report. SYSW, ACFN and JJYS critically revised the manuscript. All authors contributed to the interpretation of the data and the writing and editing of the report.

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Figure Legends

Figure 1a Correlation between age-standardised prostate cancer incidence (upper panel) and mortality (lower panel) and Human Development Index (HDI)

Figure 1b Correlation between age-standardised prostate cancer incidence (upper panel) and mortality (lower panel) and Gross Domestic Product (GDP)

Figure 2 Temporal trends in the incidence and mortality of prostate cancer in the most recent 10 years according to country

Figure 3 The Average Annual Percent Change (AAPC) of prostate cancer incidence in the most recent 10 years

Figure 4 The Average Annual Percent Change (AAPC) of prostate cancer mortality in the most recent 10 years

Supplementary Figure 1 Findings from the joinpoint regression analysis of the global incidence and mortality rates of prostate cancer

Table 1 The estimated incidence and mortality of prostate cancer according to world area, 2012

World regions	Population size (male, thousands)	Incidence		Mortality	
		n	ASR	n	ASR
Africa	549,445	59,493	23.2	42,802	17.0
Eastern Africa	180,243	17,187	23.3	13,866	18.7
Middle Africa	69,179	6,892	27.0	5,900	24.2
Northern Africa	106,147	7,548	10.6	5,000	7.0
Southern Africa	29,735	10,266	61.7	3,759	24.4
Western Africa	164,141	17,600	25.1	14,277	21.2
Asia	2,179,003	196,190	9.4	82,676	3.8
Eastern Asia	813,296	118,583	10.5	37,553	3.1
South-Eastern Asia	305,225	26,451	11.2	15,841	6.7
South-Central Asia	933,786	29,327	4.5	18,860	2.9
Western Asia	126,697	21,829	28.0	10,422	13.1
America	303,514	412,739	75.0	85,425	13.1
Caribbean	20,951	18,719	79.8	7,970	29.3
Central America	82,227	18,983	28.4	8,957	12.1
South America	200,336	114,701	60.1	34,386	16.6
North America	173,209	260,336	97.2	34,112	9.8
Europe	355,275	400,364	61.3	92,328	11.3
Central and Eastern Europe	138,249	65,432	31.3	25,862	11.6
Northern Europe	49,574	81,696	85.0	18,099	14.5
Southern Europe	74,900	91,355	58.6	20,229	9.1
Western Europe	92,553	161,881	85.8	28,138	10.7
Oceania	18,859	26,130	101.9	4,250	13.0
Australia/New Zealand	13,632	25,296	111.6	3,930	12.9
Melanesia	4,628	482	22.7	253	13.3
Micronesia/Polynesia	258	352	72.3	67	13.7
More developed regions*	604,008	741,966	68.0	142,014	10.0
Less developed regions*	2,975,297	352,950	14.5	165,467	6.6
World	3,579,305	1,094,916	30.6	307,481	7.8

ASR=Age standardized rate per 100,000. Source: GLOBOCAN 2012 [1]. Numbers are rounded to the nearest 10 or 100, and may not add up to the total. The population size of the world regions were retrieved from the Department of Economic and Social Affairs, Population Division, United Nations. Available at: http://esa.un.org/unpd/wpp/Download/Standard/Population/

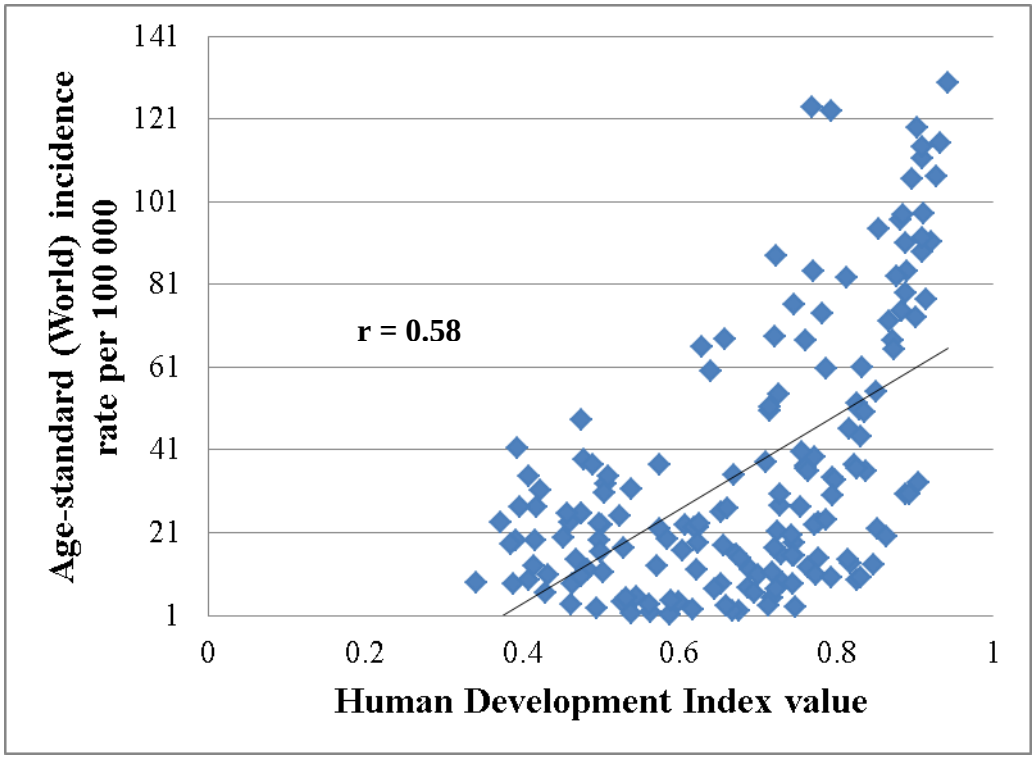
*More developed regions refer to Europe, Northern America, Australia/New Zealand and Japan. Less developed regions include all regions of Africa, Asia (except Japan), Latin America and the Caribbean plus Melanesia, Micronesia and Polynesia.

Table 2 Trends in Prostate Cancer incidence and mortality in the most recent 10 years: six groups of temporal pattern

Group A: incidence ↑, mortality↑ (3 countries)	Bulgaria※, Philippines*, Singapore
Group B: incidence↑, mortality↓ (12 countries)	Brazil※, Czech Republic, France, Ireland, Israel, Italy, Japan, Netherlands, Poland, Spain, Switzerland, The United Kingdom
Group C: Incidence↑, mortality stable (8 countries)	China, Croatia, Estonia, Latvia, Lithuania, Portugal, Slovakia, Slovenia
Group D: Incidence stable, mortality↓ (7 countries)	Australia, Austria, Colombia※, Canada, Denmark, New Zealand, Norway
Group E: Incidence stable, mortality stable (3 countries)	Costa Rica※, Iceland, Malta
Group F: incidence ↓, mortality↓ (3 countries)	Finland, Sweden, United States

*Medium Human Development Index (HDI); ※High HDI. All remaining countries had very high HDI. (Low HDI refers to HDI ≤ 0.534; Medium HDI refers to 0.534 < HDI ≤ 0.710; High HDI refers to 0.710 < HDL ≤ 0.796; and Very high HDL refers to HDI > 0.796)

Figure 1a Correlation between age-standardised prostate cancer incidence (upper panel) and mortality (lower panel) and Human Development Index (HDI)



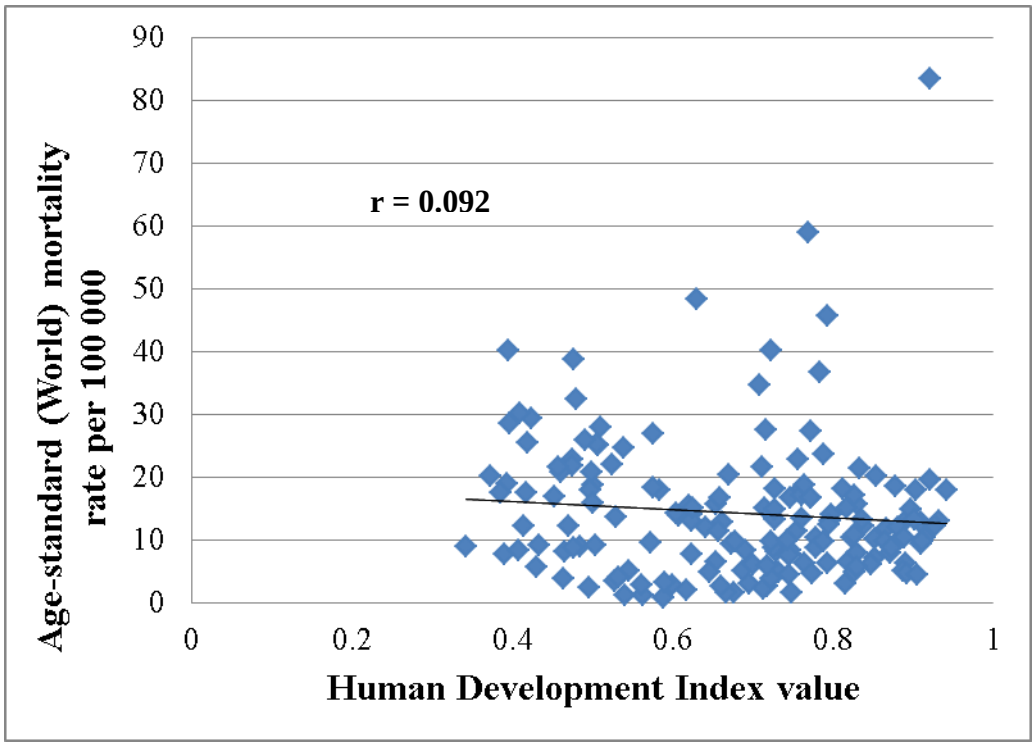
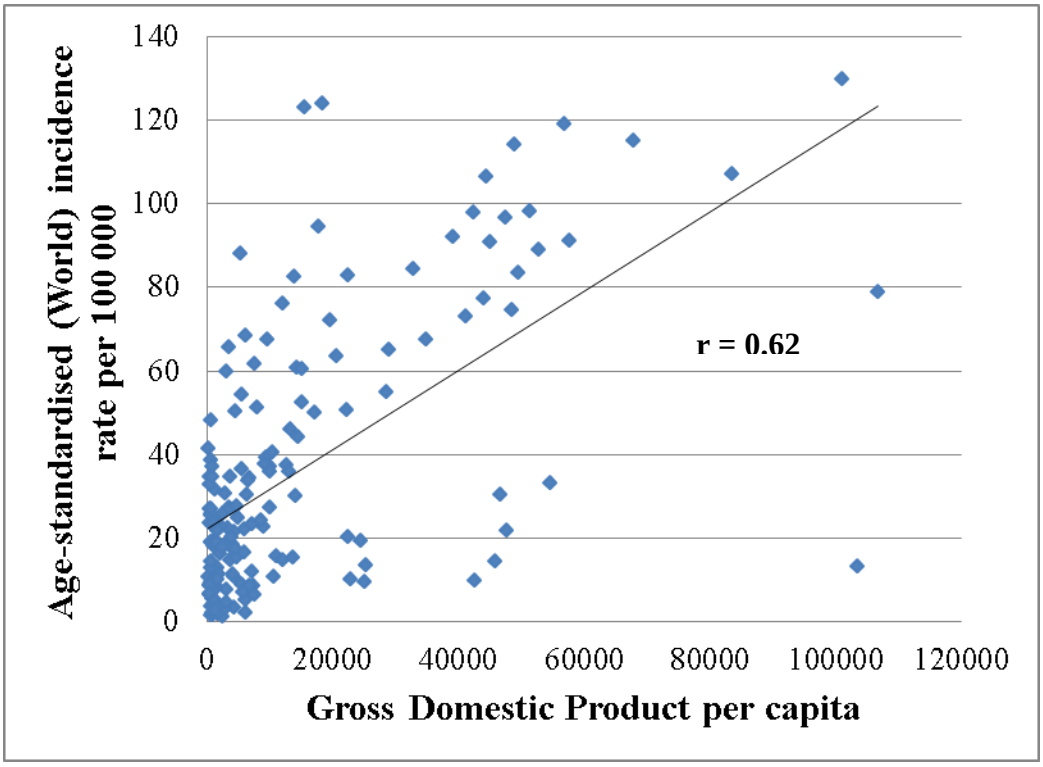


Figure 1b Correlation between age-standardized prostate cancer incidence (upper panel) and mortality (lower panel) and Gross Domestic Product (GDP)



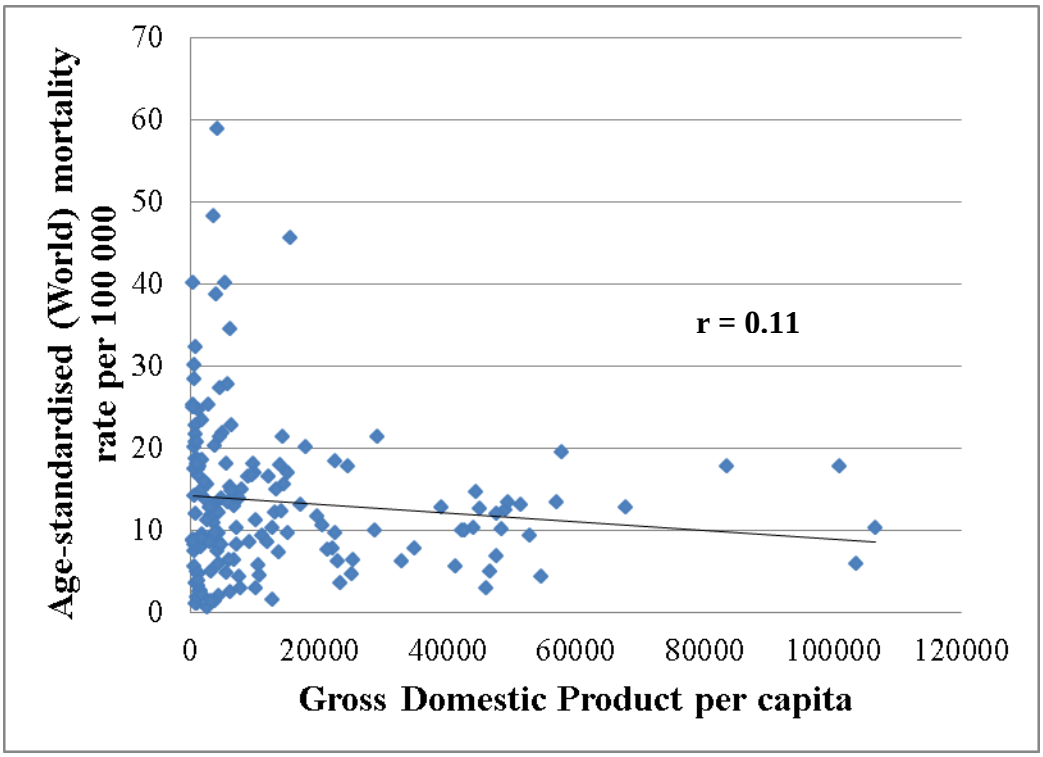
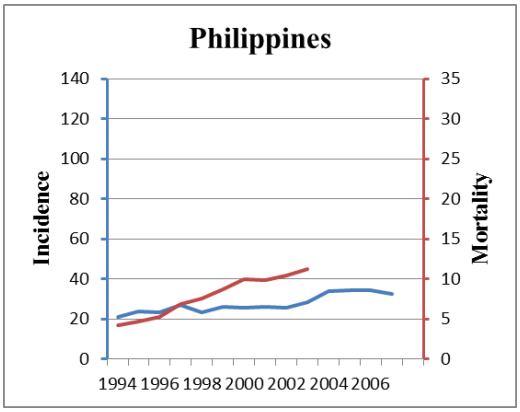
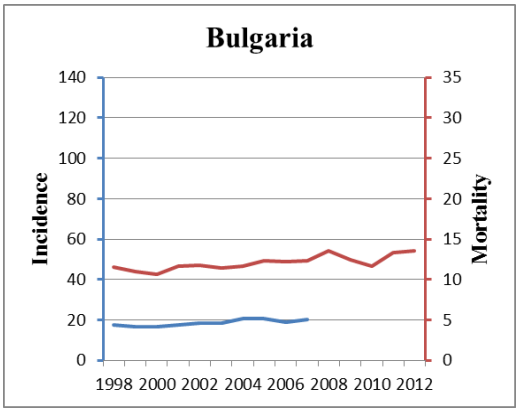
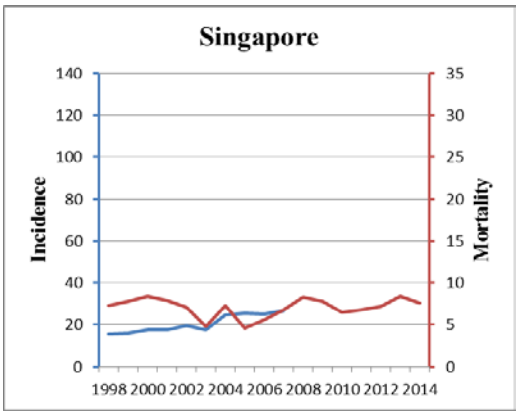


Figure 2 Temporal trends in the incidence and mortality of prostate cancer in the most recent 10 years according to country

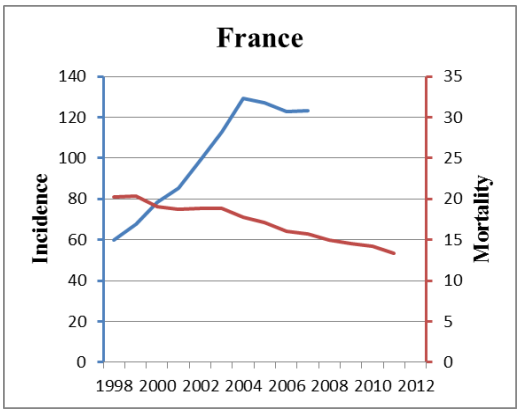
Group A: Increasing incidence and mortality

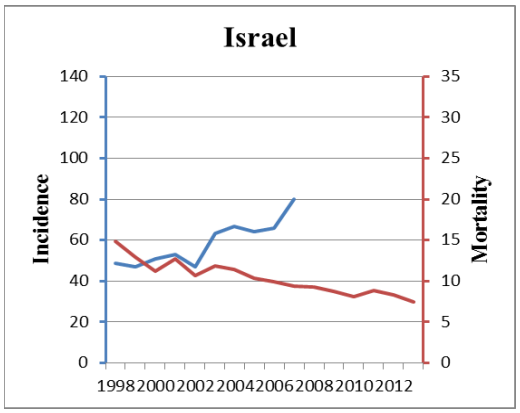


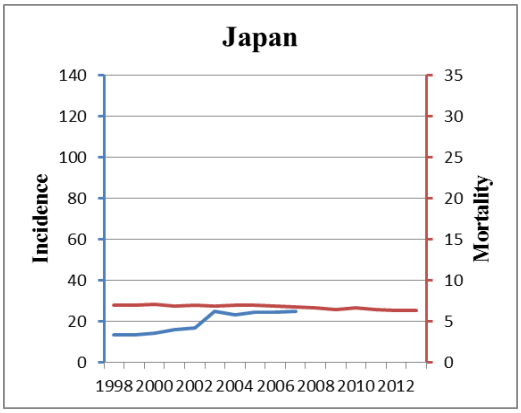


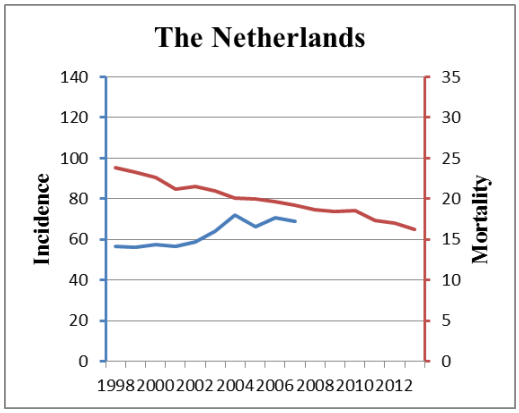


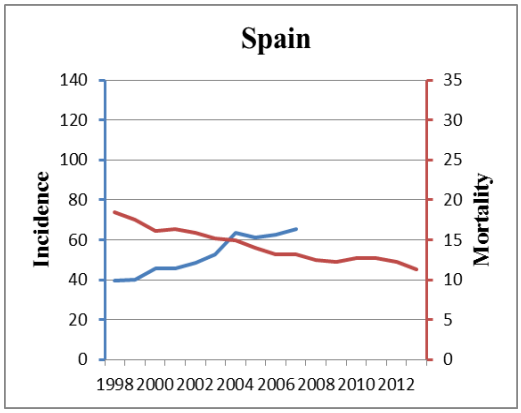
Group B: Increasing incidence and decreasing mortality

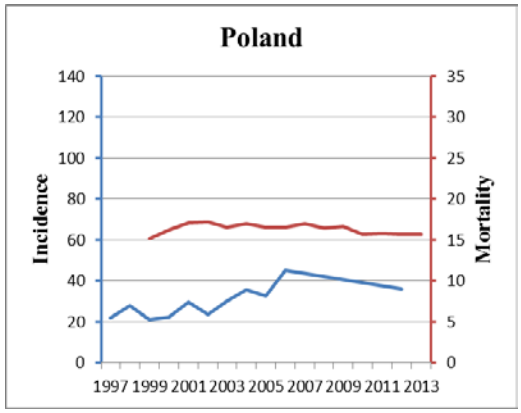


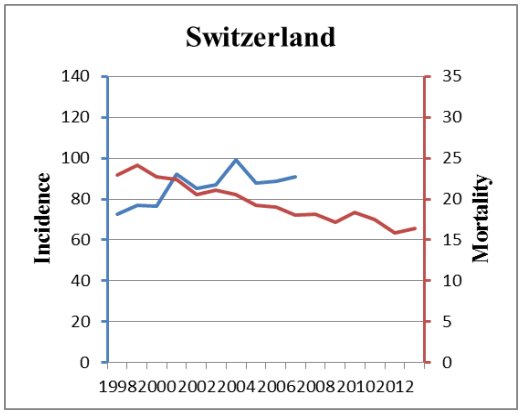


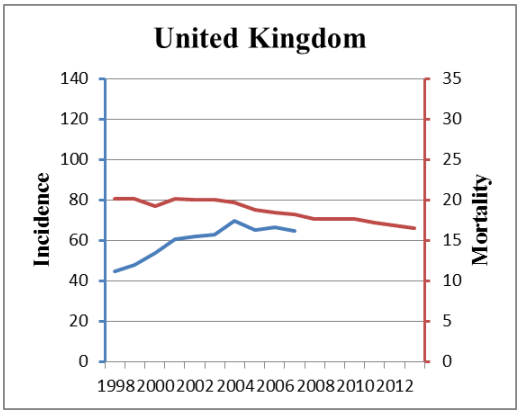

Japan
Incidence
Mortality
0 20 40 60 80 100 120 140
0 5 10 15 20 25 30 35
1998 2000 2002 2004 2006 2008 2010 2012

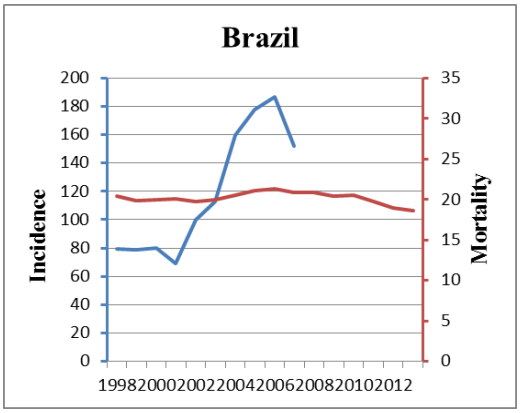

The Netherlands
Incidence
Mortality
0 20 40 60 80 100 120 140
0 5 10 15 20 25 30 35
1998 2000 2002 2004 2006 2008 2010 2012

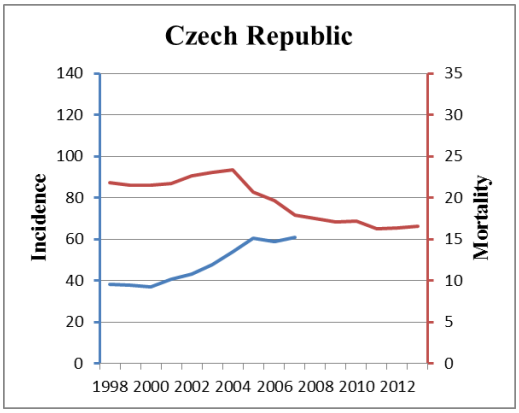

Spain
Incidence
Mortality
0 20 40 60 80 100 120 140
0 5 10 15 20 25 30 35
1998 2000 2002 2004 2006 2008 2010 2012

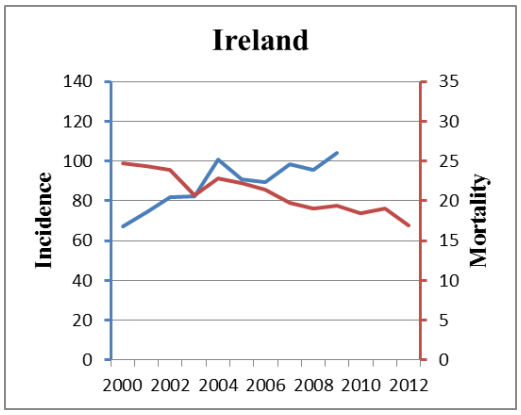

Poland
Incidence
Mortality
0 20 40 60 80 100 120 140
0 5 10 15 20 25 30 35
1997 1999 2001 2003 2005 2007 2009 2011 2013

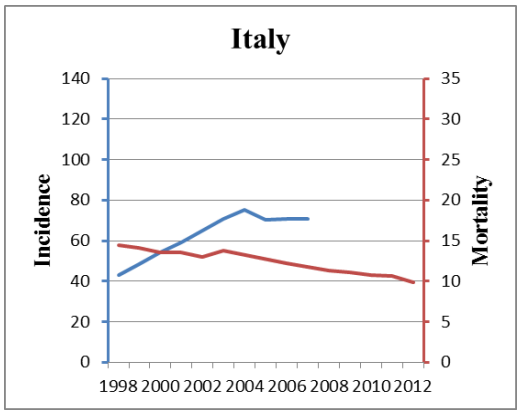

Switzerland
Incidence
Mortality
0 20 40 60 80 100 120 140
0 5 10 15 20 25 30 35
1998 2000 2002 2004 2006 2008 2010 2012


United Kingdom
Incidence
Mortality
0 20 40 60 80 100 120 140
0 5 10 15 20 25 30 35
1998 2000 2002 2004 2006 2008 2010 2012

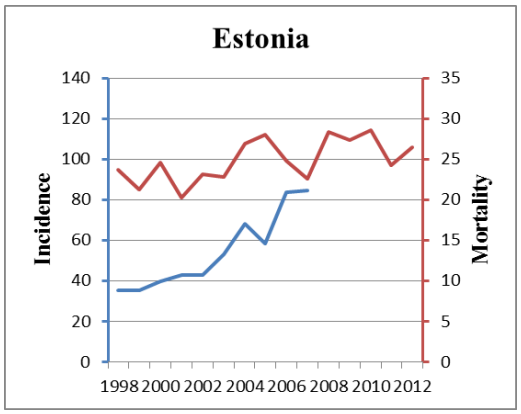

Brazil
Incidence
Mortality
0 20 40 60 80 100 120 140 160 180 200
0 5 10 15 20 25 30 35
1998 2000 2002 2004 2006 2008 2010 2012

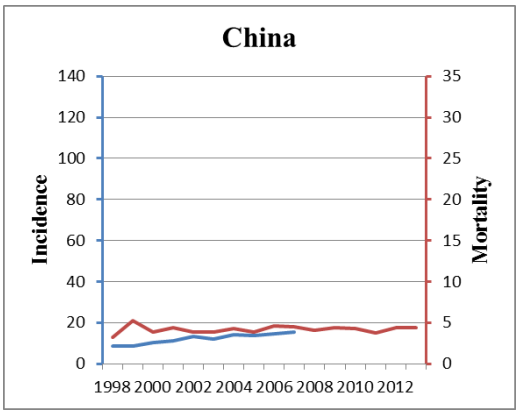

Czech Republic
Incidence
Mortality
0 20 40 60 80 100 120 140
0 5 10 15 20 25 30 35
1998 2000 2002 2004 2006 2008 2010 2012

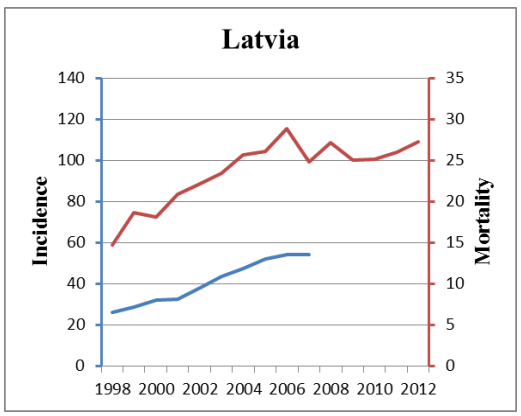


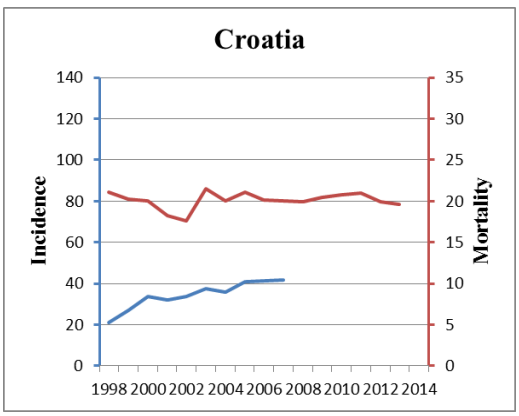


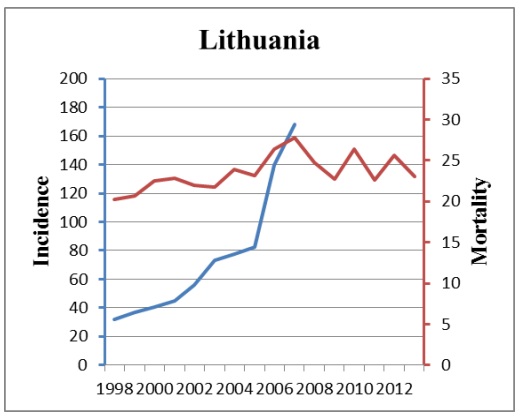
Group C: Increasing incidence and stable mortality

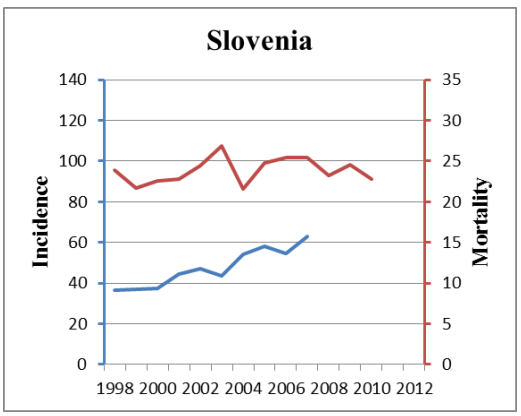


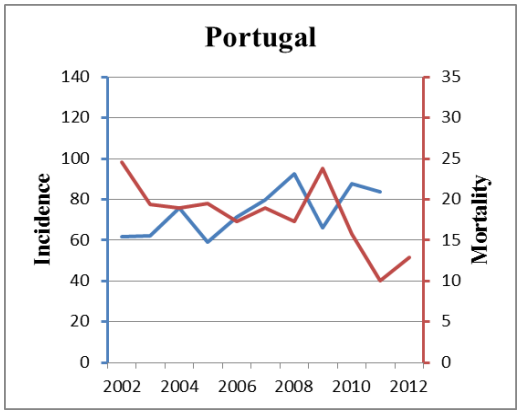




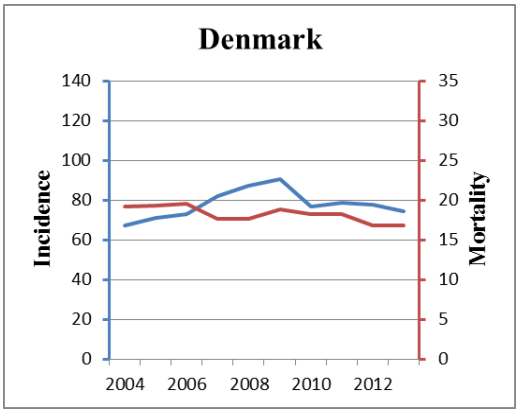


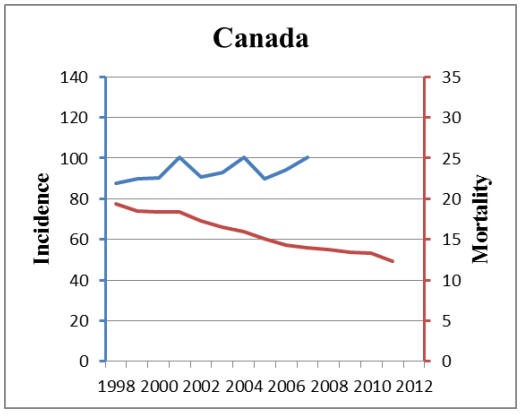


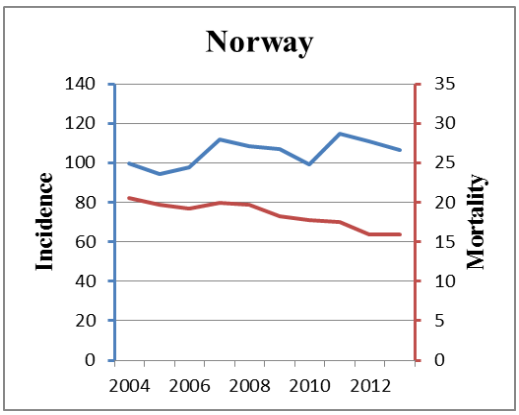


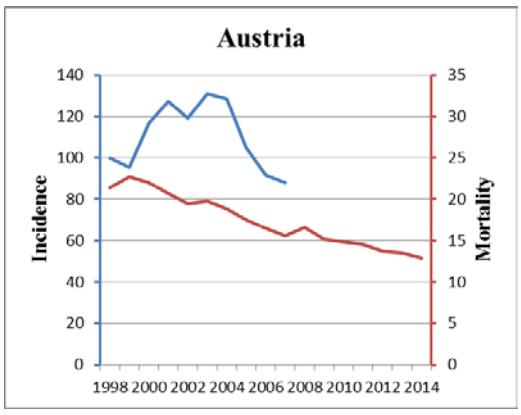


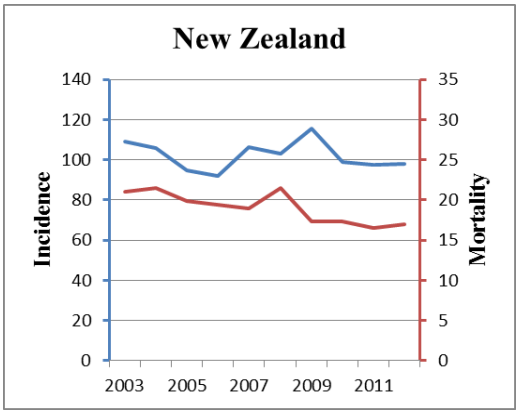
Group D: Stable incidence and decreasing mortality

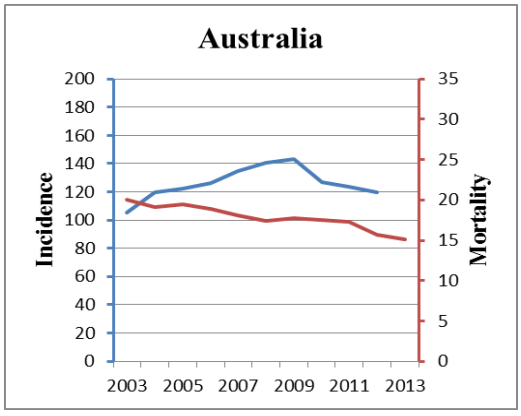


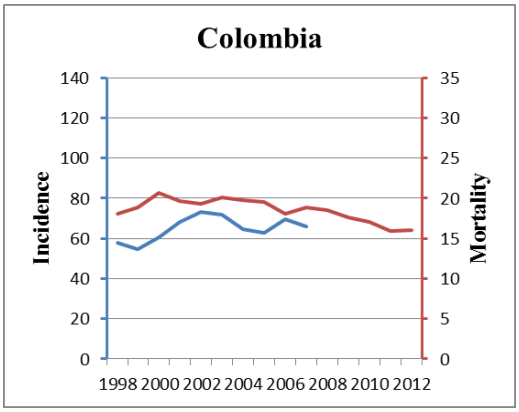




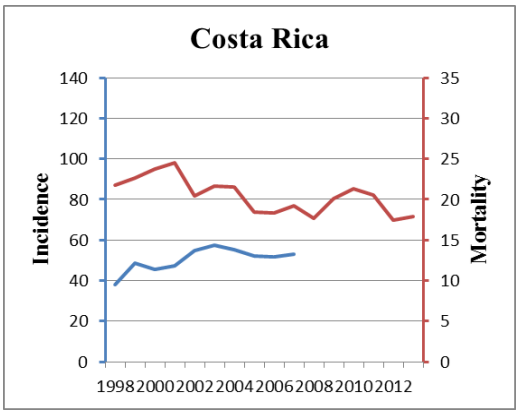


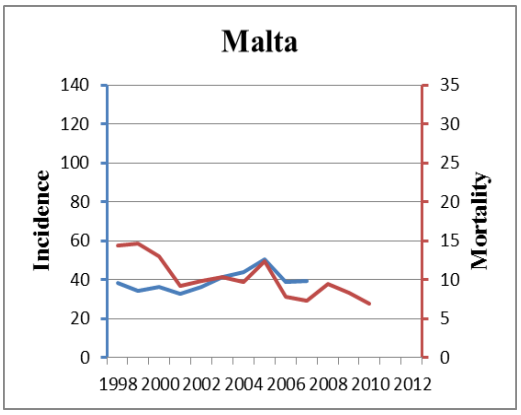


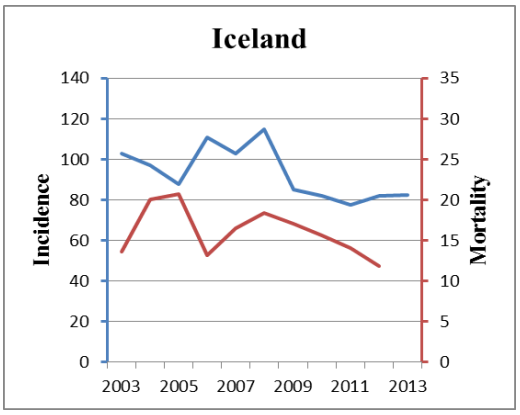




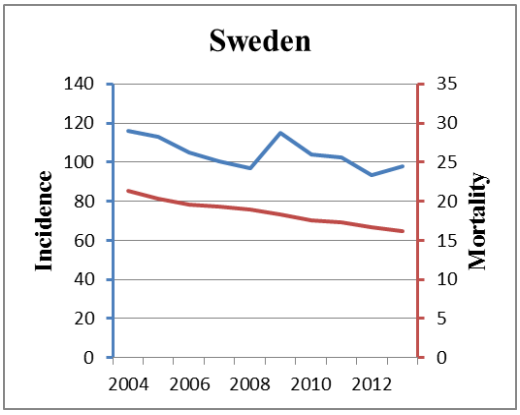
Group E: Stable incidence and mortality

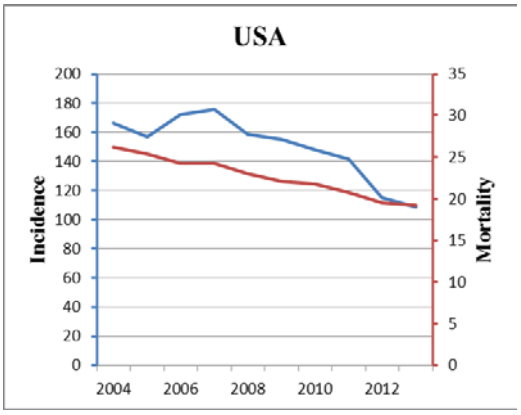


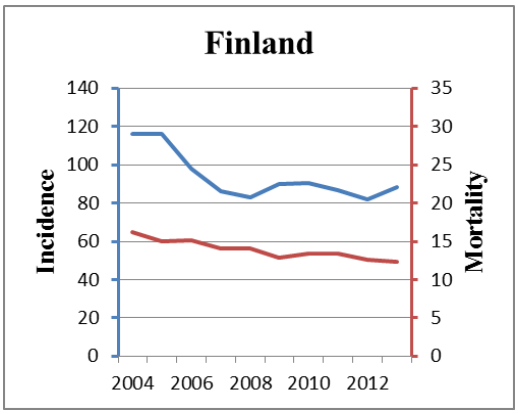


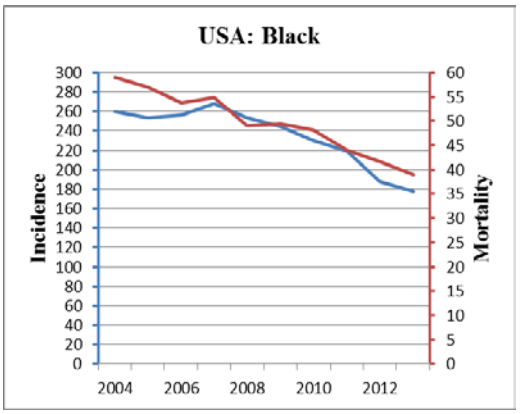


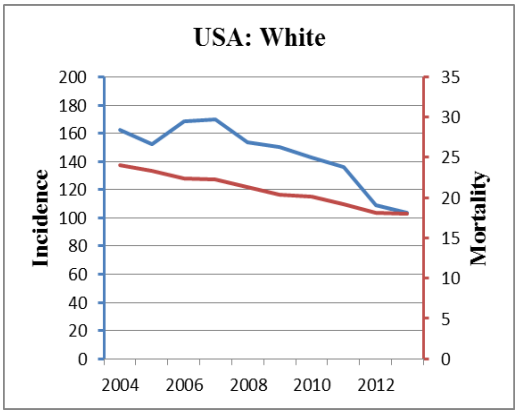
Group F: Decreasing incidence and mortality











All figures were expressed as Age-standardized rate (ASR) per 100,000. The blue line refers to incidence and red line refers to mortality. All data for incidence and mortality were retrieved from the Cancer Incidence in Five Continents series I-V and the WHO mortality database, respectively, except for US, Australia, New Zealand, Bulgaria, Ireland, Portugal, Denmark, Finland, Iceland, Norway, Sweden where country-specific registries were used as more comprehensive and updated data were available [16-20].

Figure 3 The Average Annual Percentage Change (AAPC) of prostate cancer incidence in the most recent 10 years

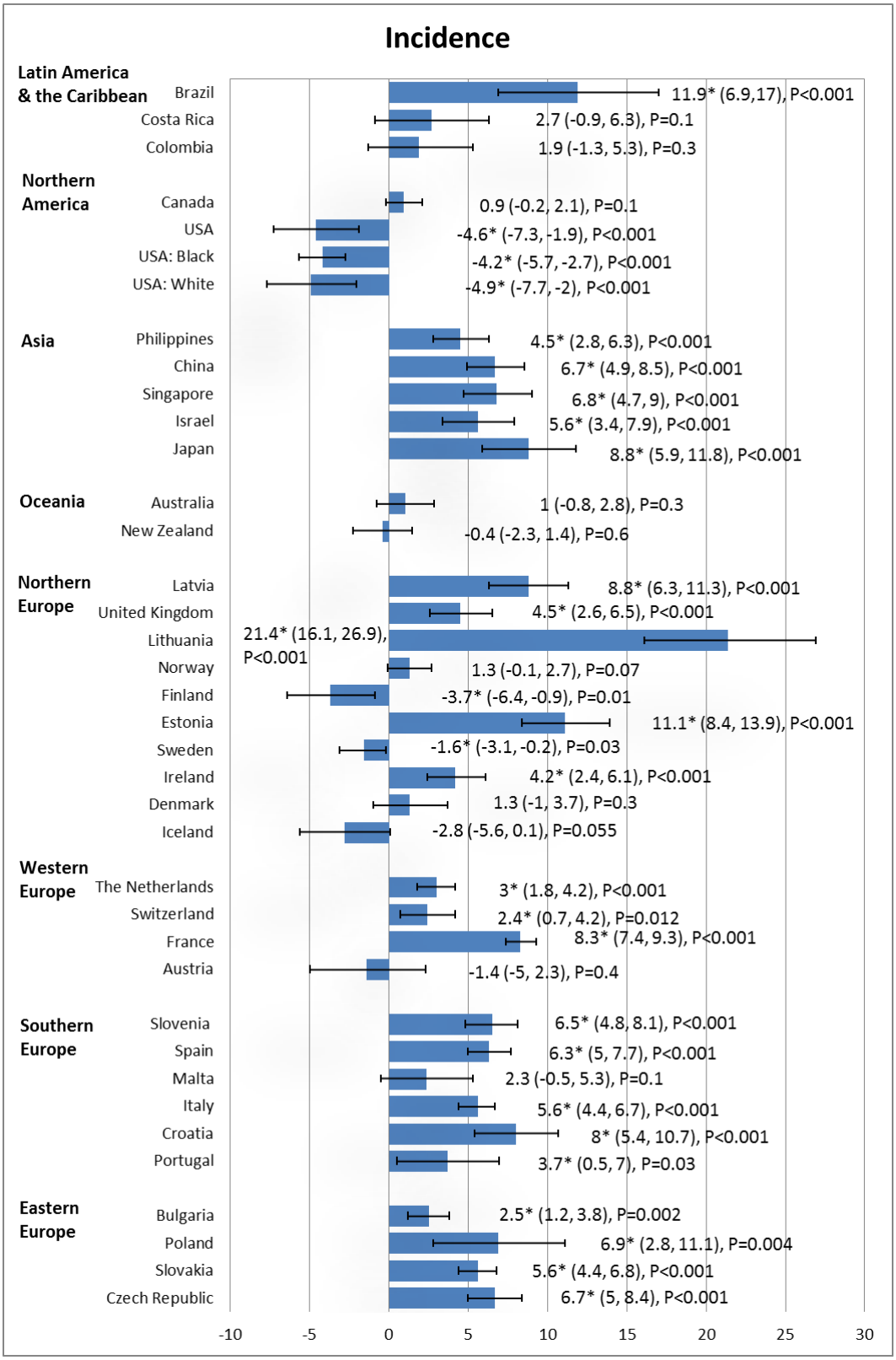
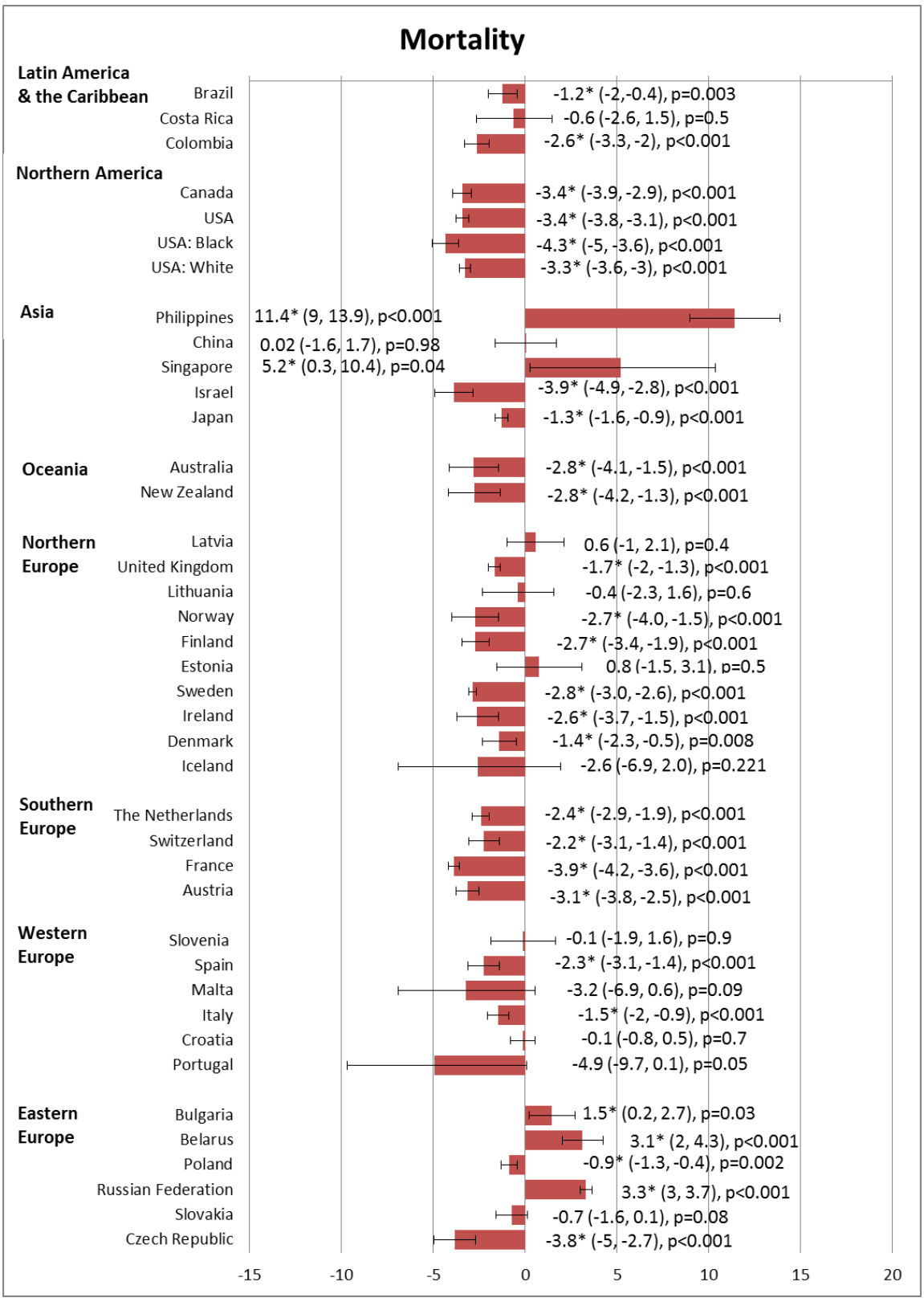
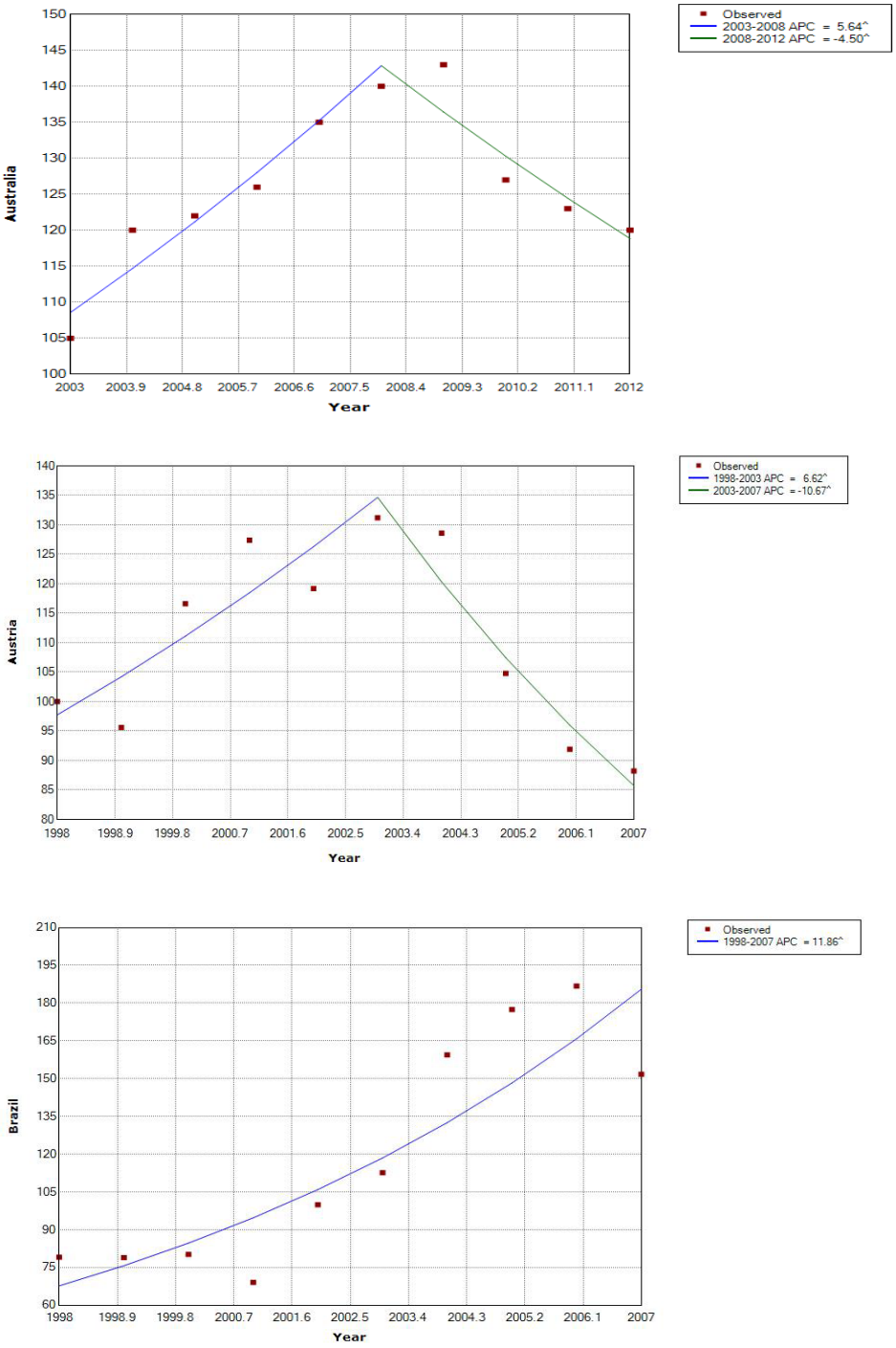


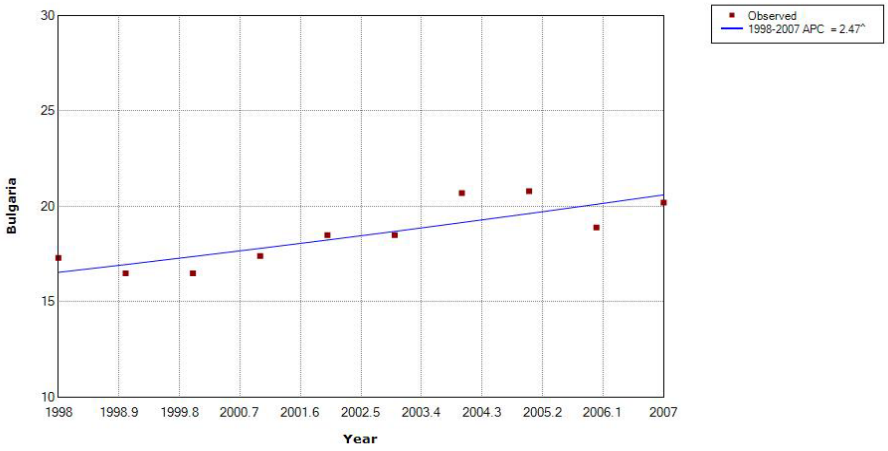
Figure 4 The Average Annual Percentage Change (AAPC) of prostate cancer mortality in the most recent 10 years

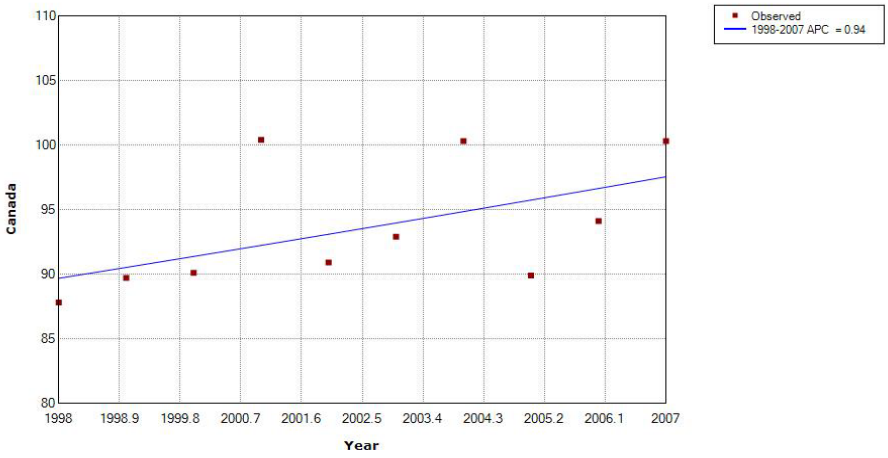


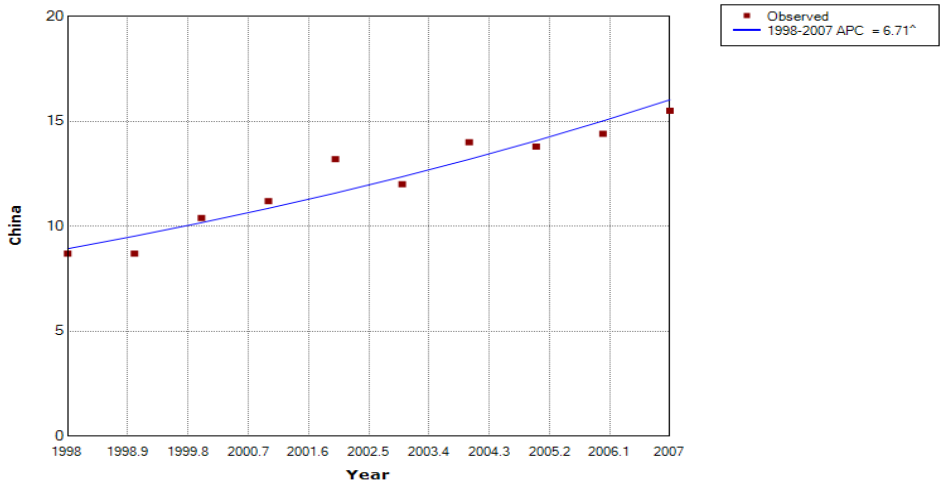
Supplementary Figure 1 Findings from the joinpoint regression analysis of the global incidence and mortality rates of prostate cancer

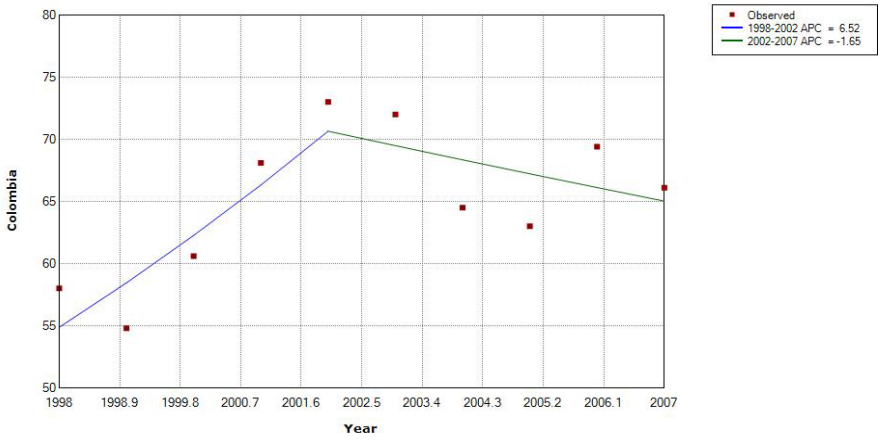
(A). Incidence

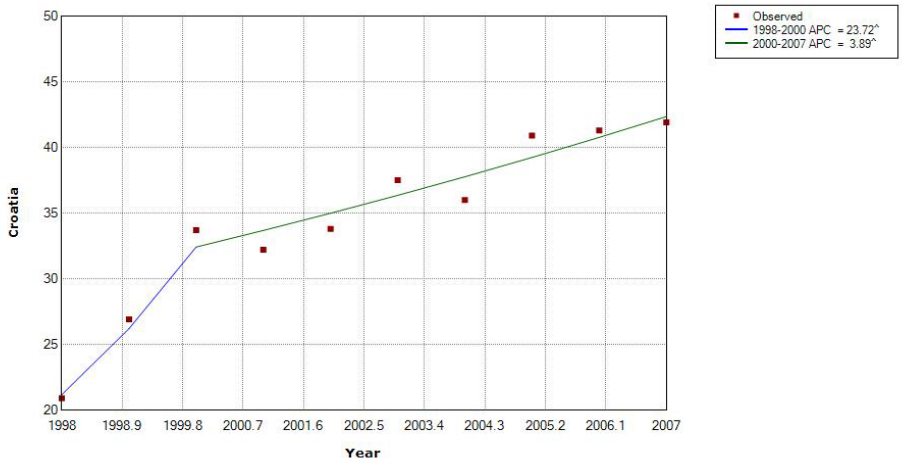


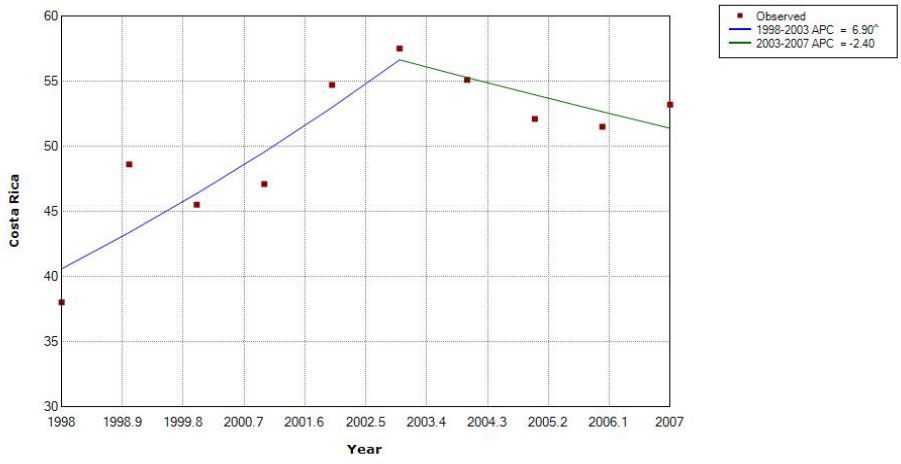

Observed
1998-2007 APC = 2.47^
Bulgaria
30
25
20
15
10
1998
1998.9
1999.8
2000.7
2001.6
2002.5
2003.4
2004.3
2005.2
2006.1
2007
Year

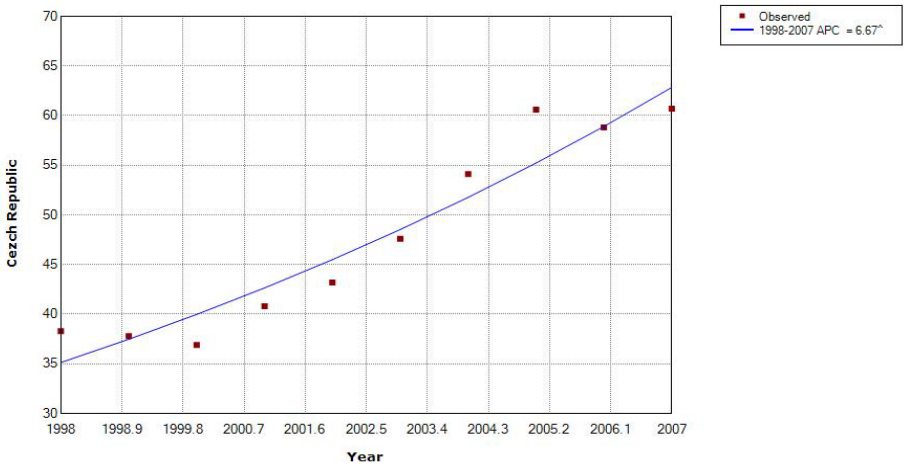

Observed
1998-2007 APC = 0.94
Canada
110
105
100
95
90
85
80
1998
1998.9
1999.8
2000.7
2001.6
2002.5
2003.4
2004.3
2005.2
2006.1
2007
Year

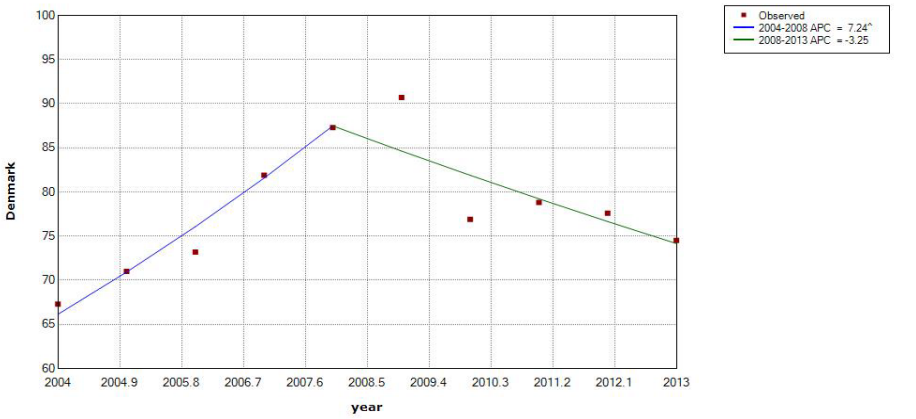

Observed
1998-2007 APC = 6.71^
China
20
15
10
5
0
1998
1998.9
1999.8
2000.7
2001.6
2002.5
2003.4
2004.3
2005.2
2006.1
2007
Year

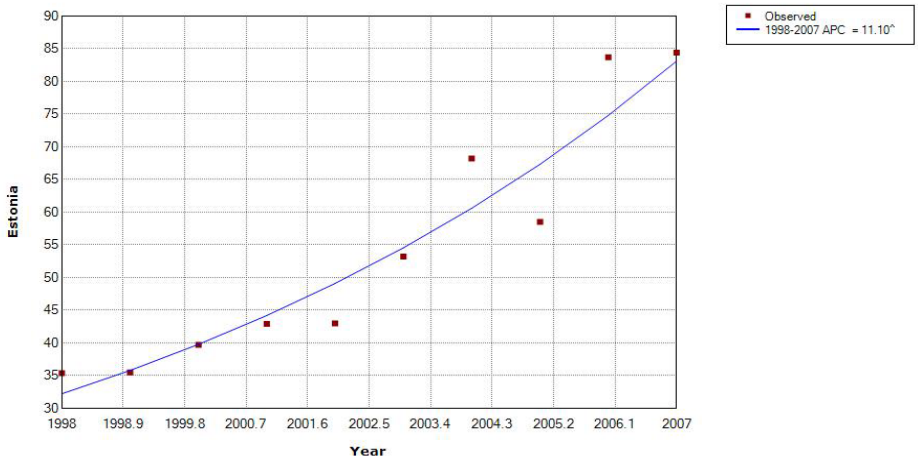

Observed
1998-2002 APC = 6.52
2002-2007 APC = -1.65
Colombia
Year
80
75
70
65
60
55
50
1998
1998.9
1999.8
2000.7
2001.6
2002.5
2003.4
2004.3
2005.2
2006.1
2007

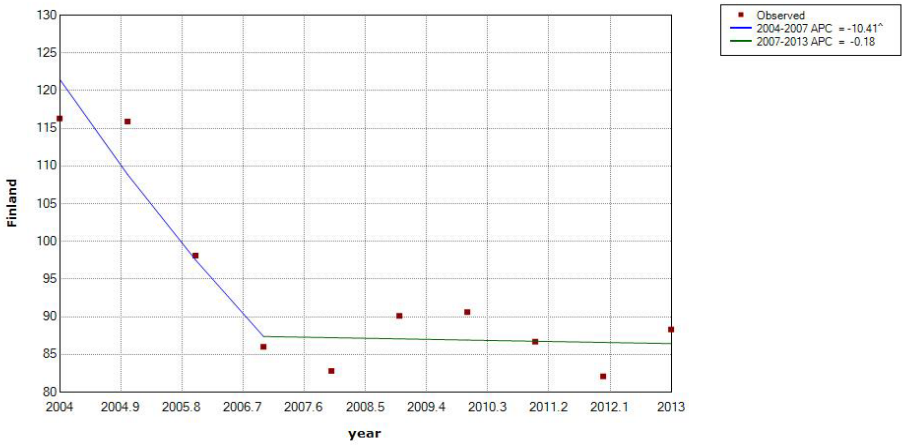

Observed
1998-2000 APC = 23.72^
2000-2007 APC = 3.89^
Croatia
Year
50
45
40
35
30
25
20
1998
1998.9
1999.8
2000.7
2001.6
2002.5
2003.4
2004.3
2005.2
2006.1
2007

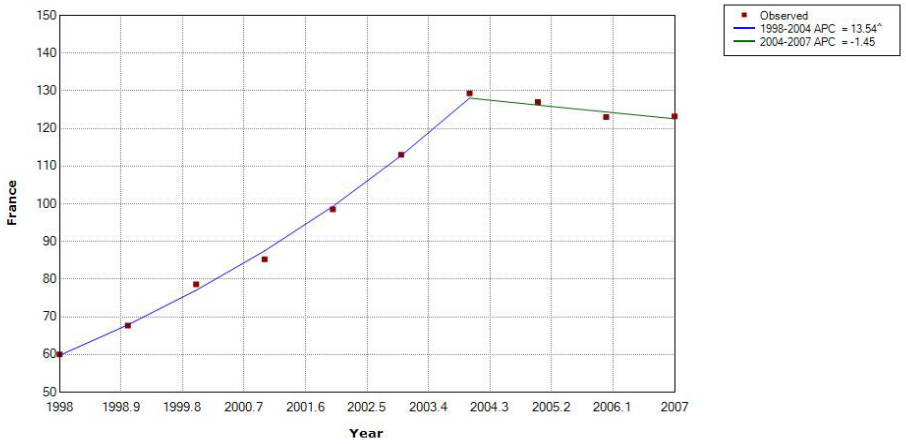

Observed
1998-2003 APC = 6.90^
2003-2007 APC = -2.40
Costa Rica
Year
60
55
50
45
40
35
30
1998
1998.9
1999.8
2000.7
2001.6
2002.5
2003.4
2004.3
2005.2
2006.1
2007

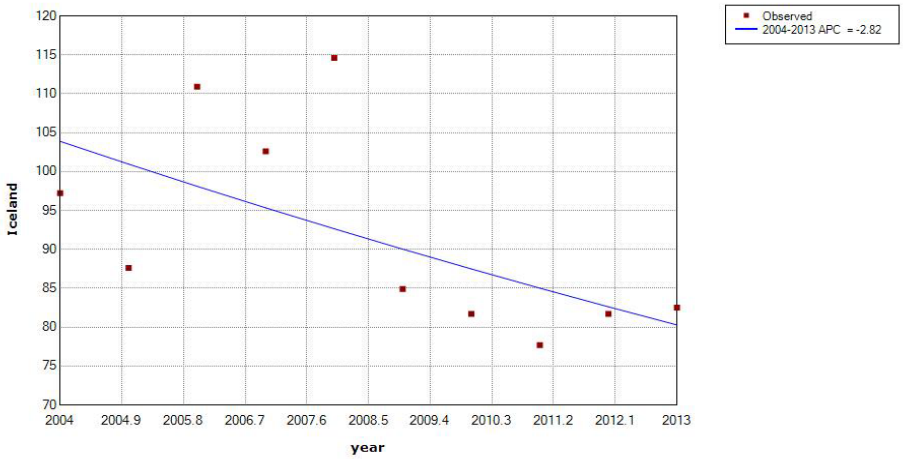

Observed
1998-2007 APC = 6.67^
Cezch Republic
70
65
60
55
50
45
40
35
30
1998
1998.9
1999.8
2000.7
2001.6
2002.5
2003.4
2004.3
2005.2
2006.1
2007
Year

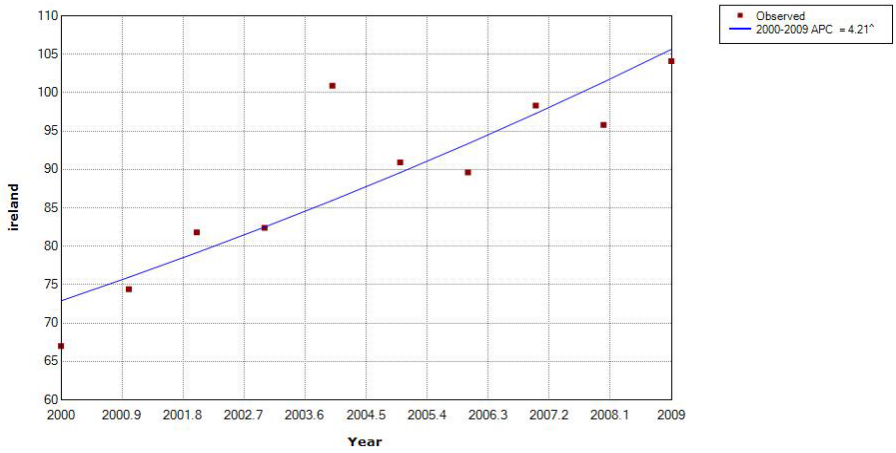

Observed
2004-2008 APC = 7.24^
2008-2013 APC = -3.25
Denmark
100
95
90
85
80
75
70
65
60
2004
2004.9
2005.8
2006.7
2007.6
2008.5
2009.4
2010.3
2011.2
2012.1
2013
year

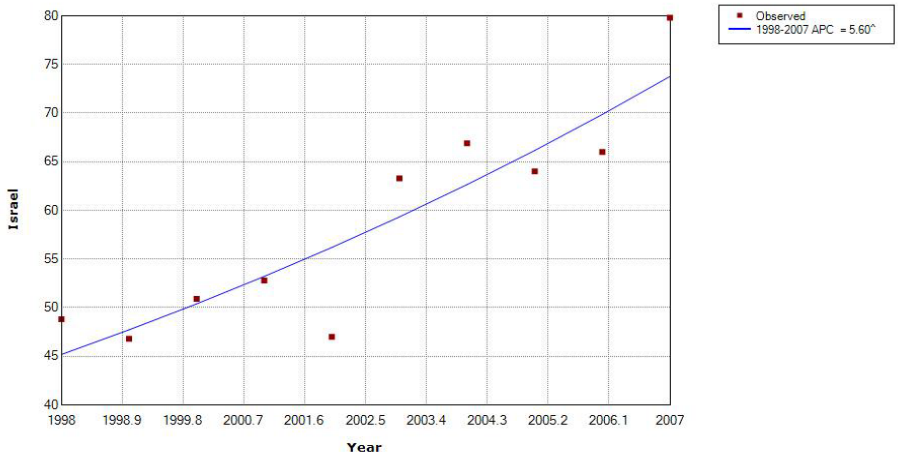

Observed
1998-2007 APC = 11.10^
Estonia
90
85
80
75
70
65
60
55
50
45
40
35
30
1998
1998.9
1999.8
2000.7
2001.6
2002.5
2003.4
2004.3
2005.2
2006.1
2007
Year

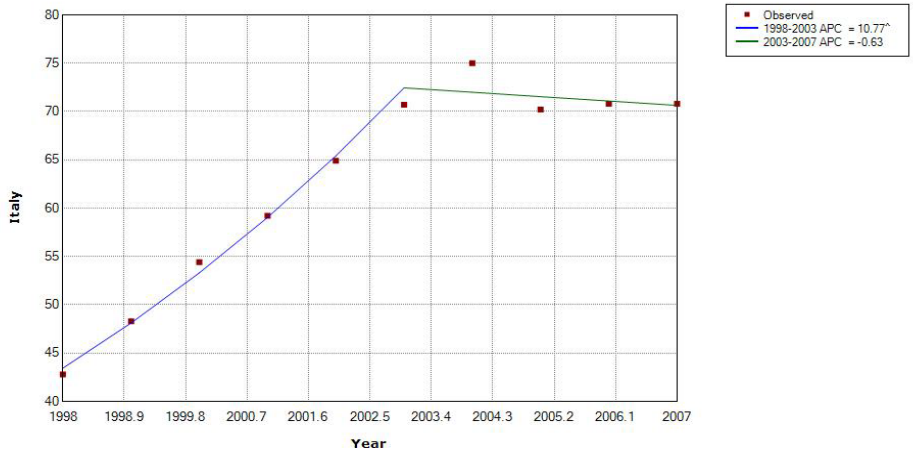

Observed
2004-2007 APC = -10.41^
2007-2013 APC = -0.18
Finland
year

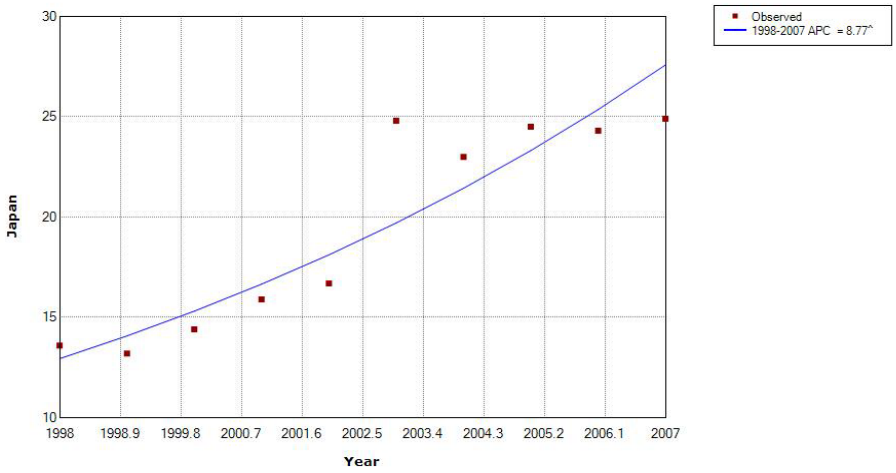

Observed
1998-2004 APC = 13.54^
2004-2007 APC = -1.45
France
Year

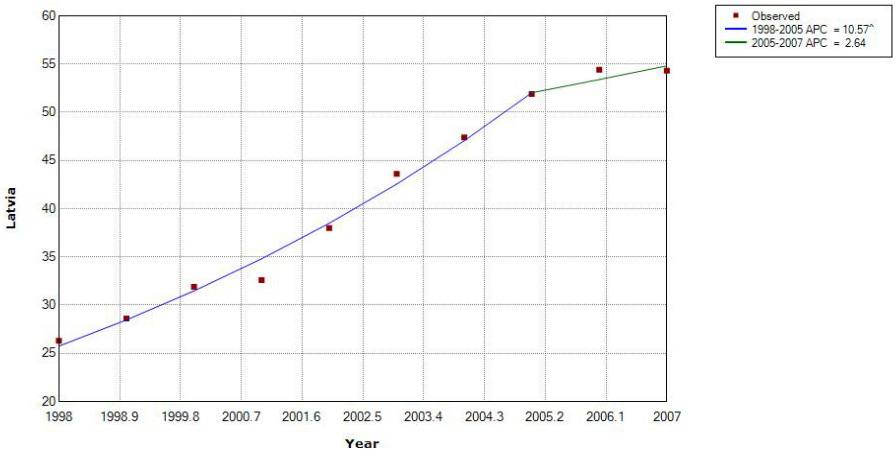

Observed
2004-2013 APC = -2.82
Iceland
year

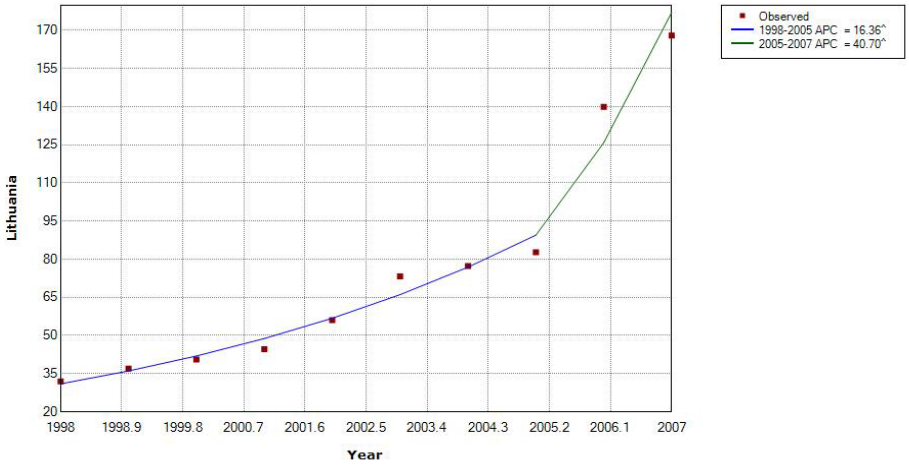

Observed
2000-2009 APC = 4.21^
ireland
110
105
100
95
90
85
80
75
70
65
60
2000
2000.9
2001.8
2002.7
2003.6
2004.5
2005.4
2006.3
2007.2
2008.1
2009
Year

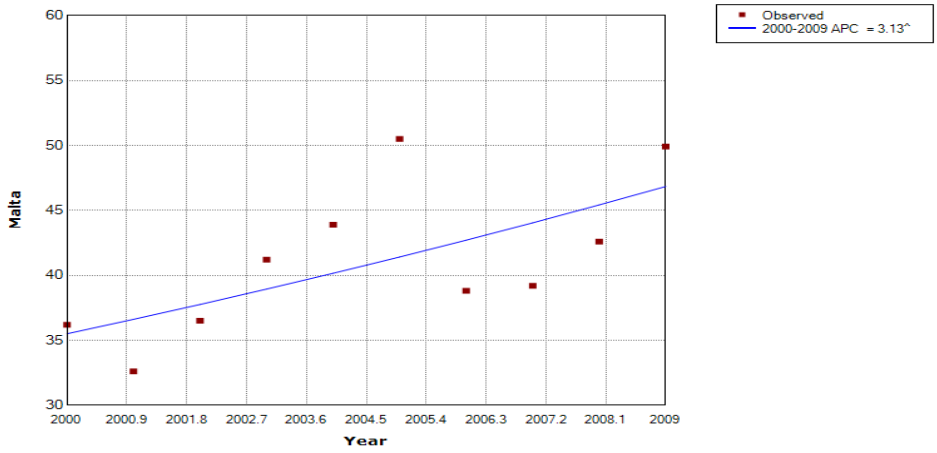

Observed
1998-2007 APC = 5.60^
Israel
80
75
70
65
60
55
50
45
40
1998
1998.9
1999.8
2000.7
2001.6
2002.5
2003.4
2004.3
2005.2
2006.1
2007
Year

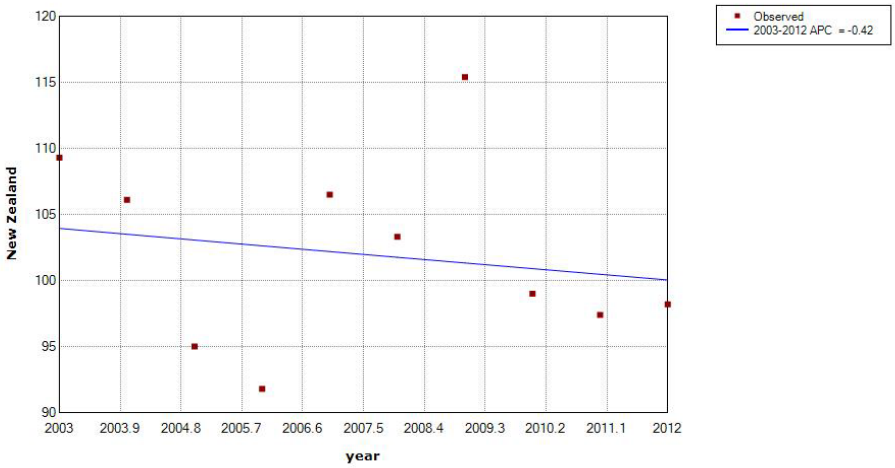

Observed
1998-2003 APC = 10.77^
2003-2007 APC = -0.63
Italy
80
75
70
65
60
55
50
45
40
1998
1998.9
1999.8
2000.7
2001.6
2002.5
2003.4
2004.3
2005.2
2006.1
2007
Year

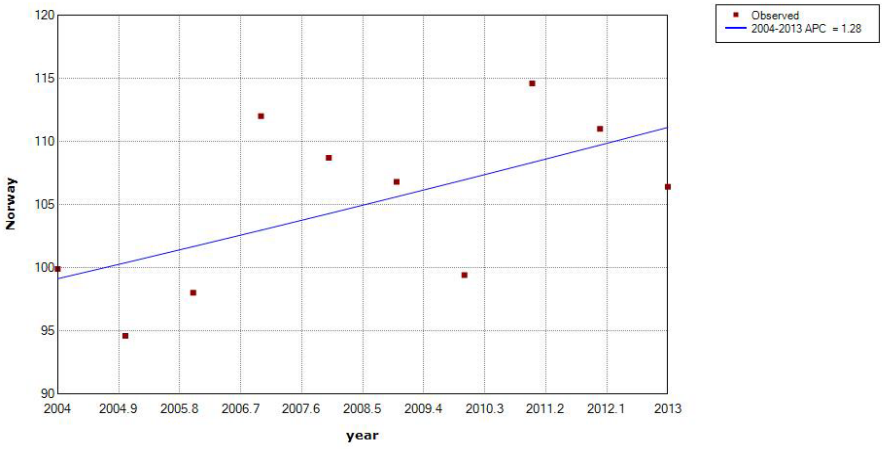

Observed
1998-2007 APC = 8.77^
Japan
Year
30
25
20
15
10
1998
1998.9
1999.8
2000.7
2001.6
2002.5
2003.4
2004.3
2005.2
2006.1
2007

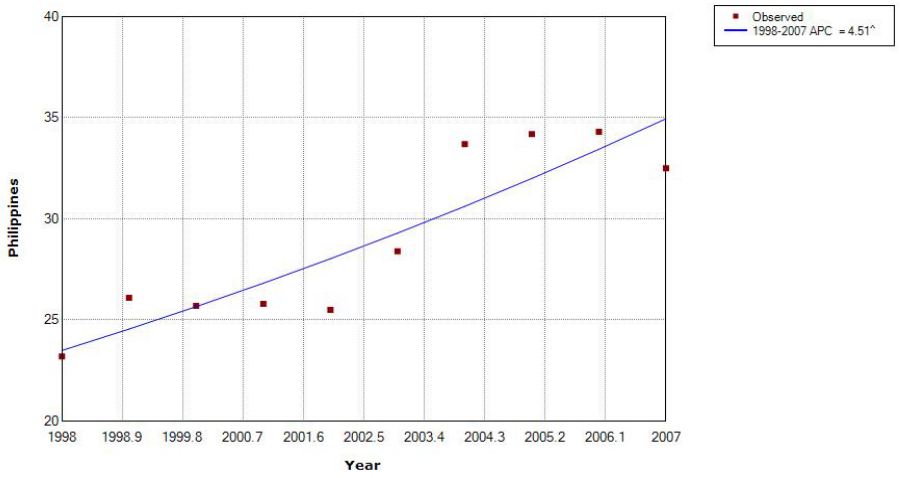

Observed
1998-2005 APC = 10.57^
2005-2007 APC = 2.64
Latvia
Year
60
55
50
45
40
35
30
25
20
1998
1998.9
1999.8
2000.7
2001.6
2002.5
2003.4
2004.3
2005.2
2006.1
2007

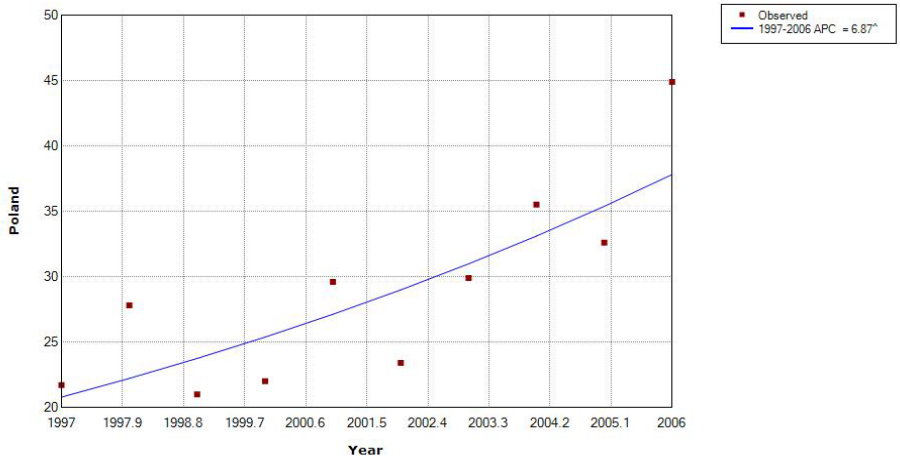

Observed
1998-2005 APC = 16.36^
2005-2007 APC = 40.70^
Lithuania
Year
170
155
140
125
110
95
80
65
50
35
20
1998
1998.9
1999.8
2000.7
2001.6
2002.5
2003.4
2004.3
2005.2
2006.1
2007

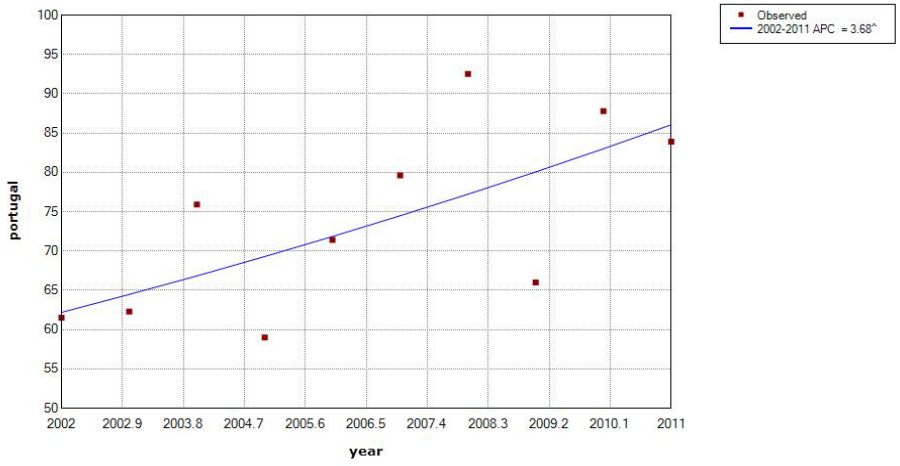

Observed
2000-2009 APC = 3.13^
Malta
Year
60
55
50
45
40
35
30
2000
2000.9
2001.8
2002.7
2003.6
2004.5
2005.4
2006.3
2007.2
2008.1
2009

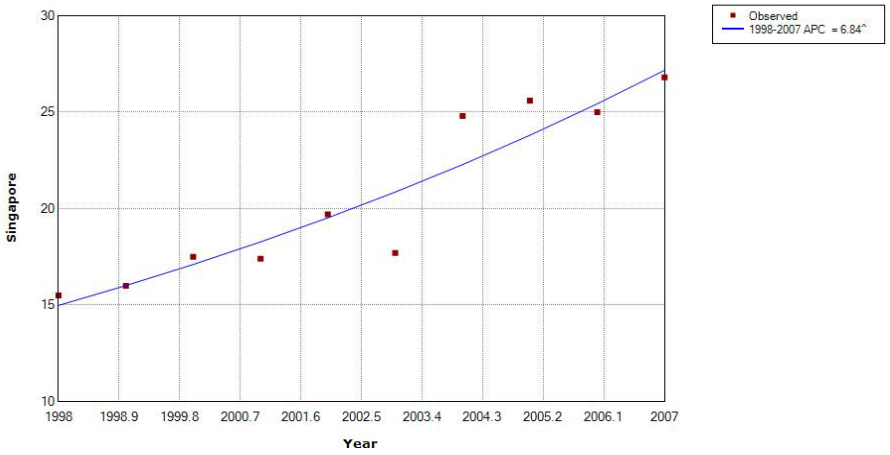

Observed
2003-2012 APC = -0.42
New Zealand
year
120
115
110
105
100
95
90
2003
2003.9
2004.8
2005.7
2006.6
2007.5
2008.4
2009.3
2010.2
2011.1
2012

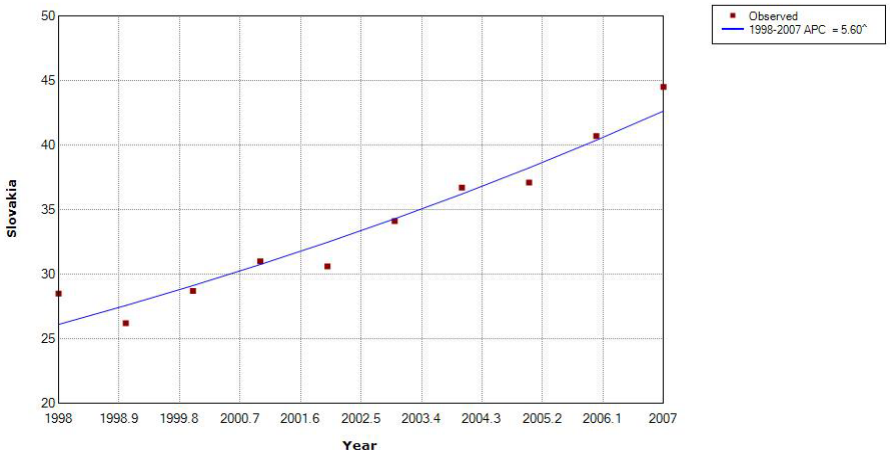

Observed
2004-2013 APC = 1.28
Norway
year
120
115
110
105
100
95
90
2004
2004.9
2005.8
2006.7
2007.6
2008.5
2009.4
2010.3
2011.2
2012.1
2013

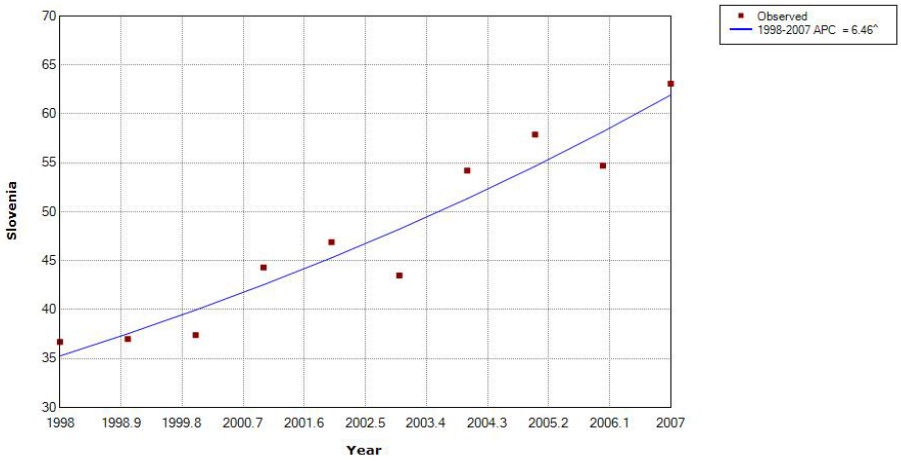

Observed
1998-2007 APC = 4.51^
Philippines
Year
40
35
30
25
20
1998
1998.9
1999.8
2000.7
2001.6
2002.5
2003.4
2004.3
2005.2
2006.1
2007

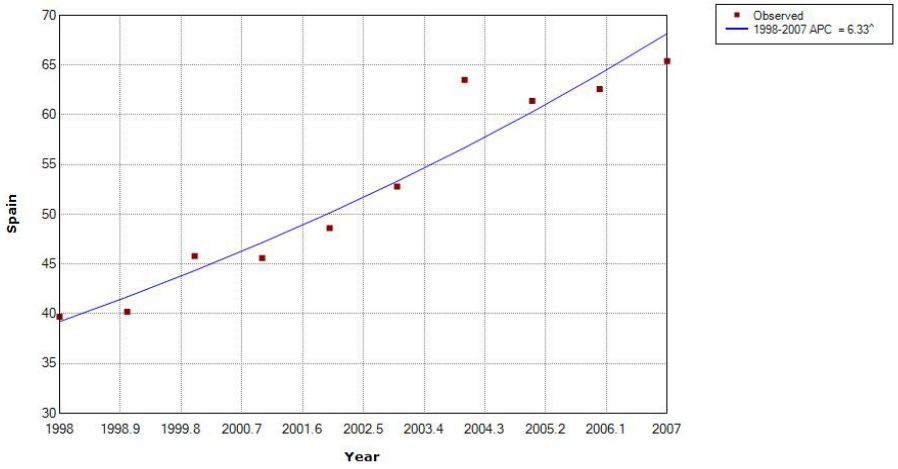

Observed
1997-2006 APC = 6.87^
Poland
Year
50
45
40
35
30
25
20
1997
1997.9
1998.8
1999.7
2000.6
2001.5
2002.4
2003.3
2004.2
2005.1
2006

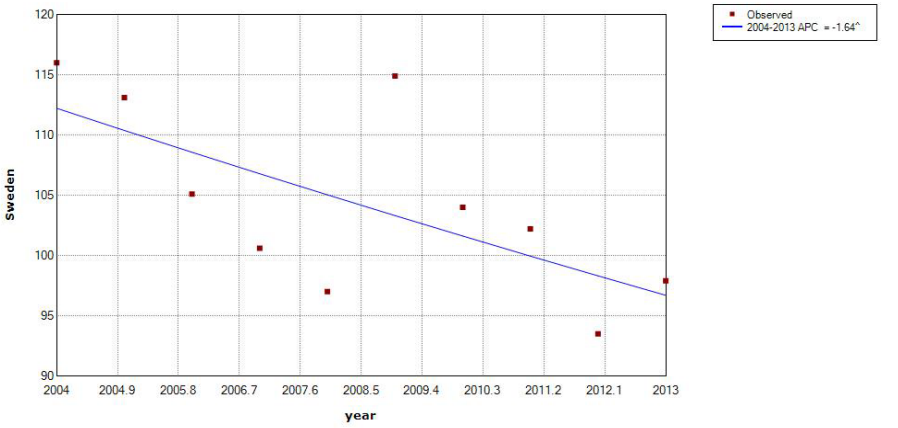

Observed
2002-2011 APC = 3.68^
portugal
year
100
95
90
85
80
75
70
65
60
55
50
2002
2002.9
2003.8
2004.7
2005.6
2006.5
2007.4
2008.3
2009.2
2010.1
2011

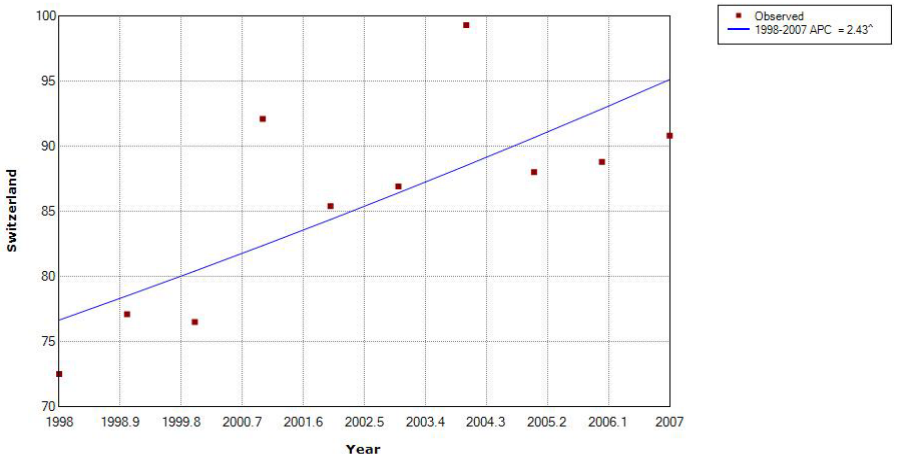

Observed
1998-2007 APC = 6.84^
Singapore
30
25
20
15
10
1998
1998.9
1999.8
2000.7
2001.6
2002.5
2003.4
2004.3
2005.2
2006.1
2007
Year

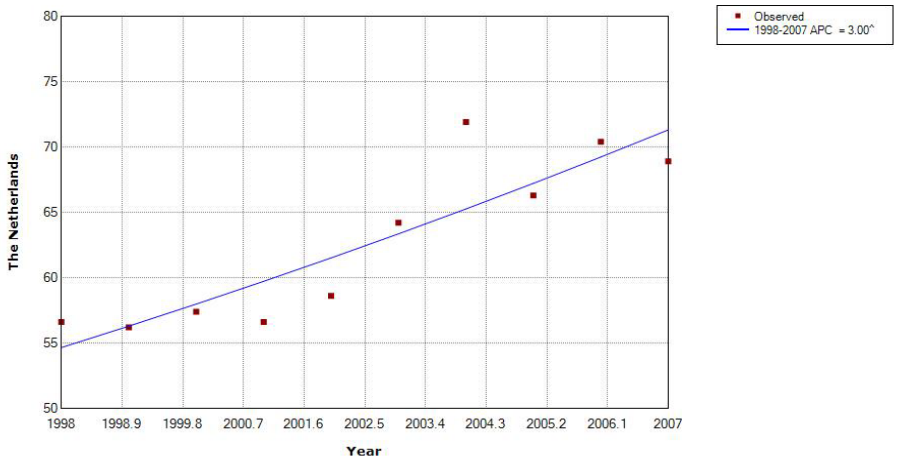

Observed
1998-2007 APC = 5.60^
Slovakia
50
45
40
35
30
25
20
1998
1998.9
1999.8
2000.7
2001.6
2002.5
2003.4
2004.3
2005.2
2006.1
2007
Year

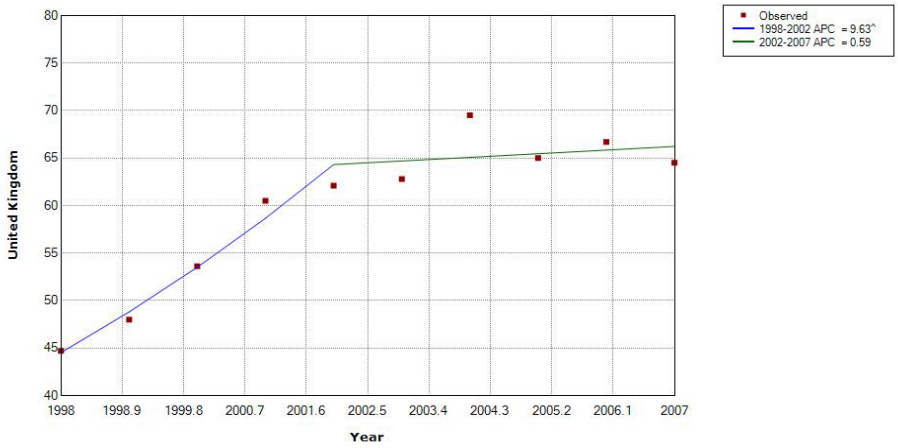

Observed
1998-2007 APC = 6.46^
Slovenia
70
65
60
55
50
45
40
35
30
1998
1998.9
1999.8
2000.7
2001.6
2002.5
2003.4
2004.3
2005.2
2006.1
2007
Year

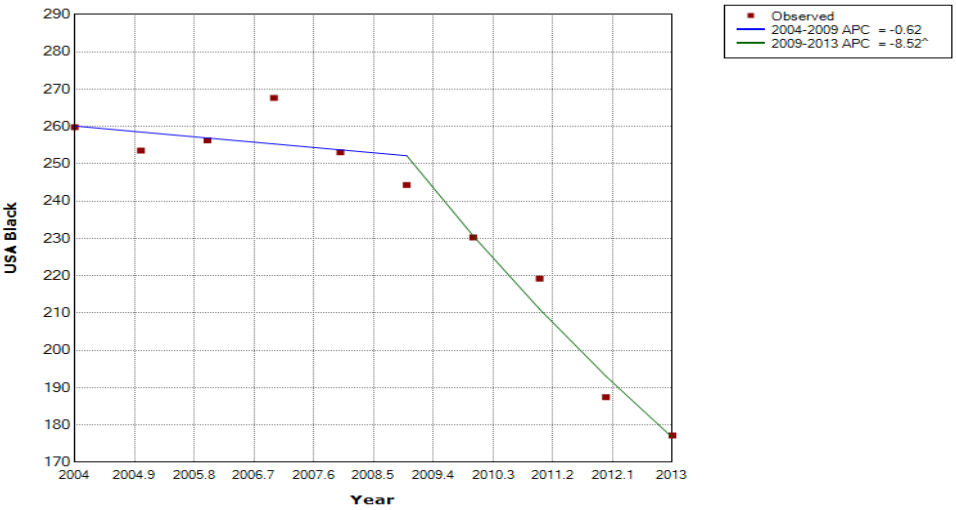

Observed
1998-2007 APC = 6.33^
Spain
Year
70
65
60
55
50
45
40
35
30
1998
1998.9
1999.8
2000.7
2001.6
2002.5
2003.4
2004.3
2005.2
2006.1
2007

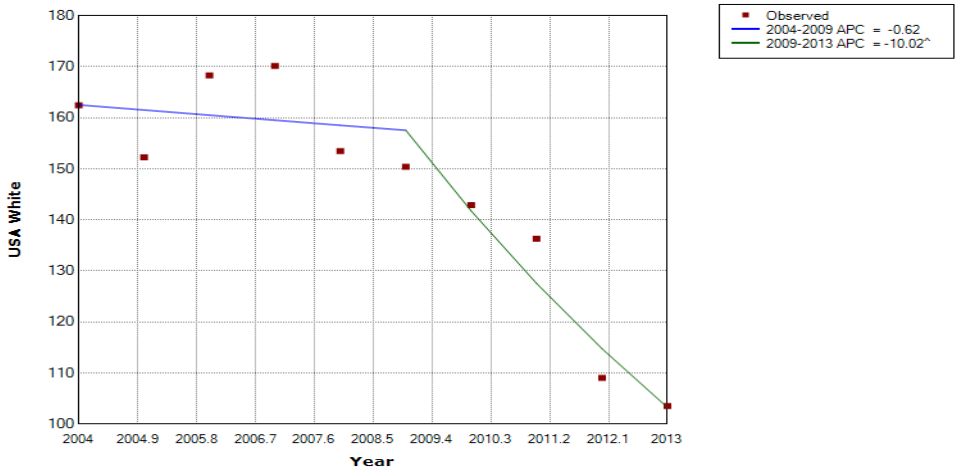

Observed
2004-2013 APC = -1.64^
Sweden
year
120
115
110
105
100
95
90
2004
2004.9
2005.8
2006.7
2007.6
2008.5
2009.4
2010.3
2011.2
2012.1
2013

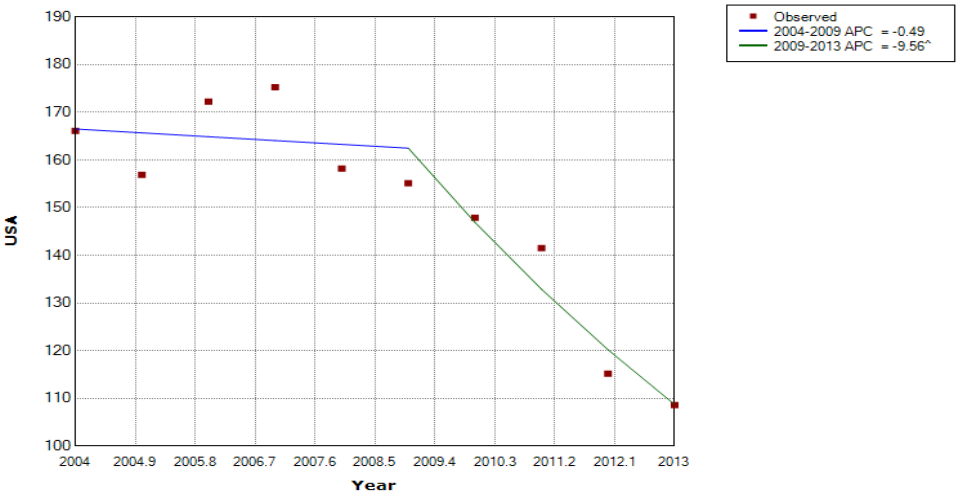

Observed
1998-2007 APC = 2.43^
Switzerland
Year
100
95
90
85
80
75
70
1998
1998.9
1999.8
2000.7
2001.6
2002.5
2003.4
2004.3
2005.2
2006.1
2007


Observed
1998-2007 APC = 3.00^
The Netherlands
80
75
70
65
60
55
50
1998
1998.9
1999.8
2000.7
2001.6
2002.5
2003.4
2004.3
2005.2
2006.1
2007
Year

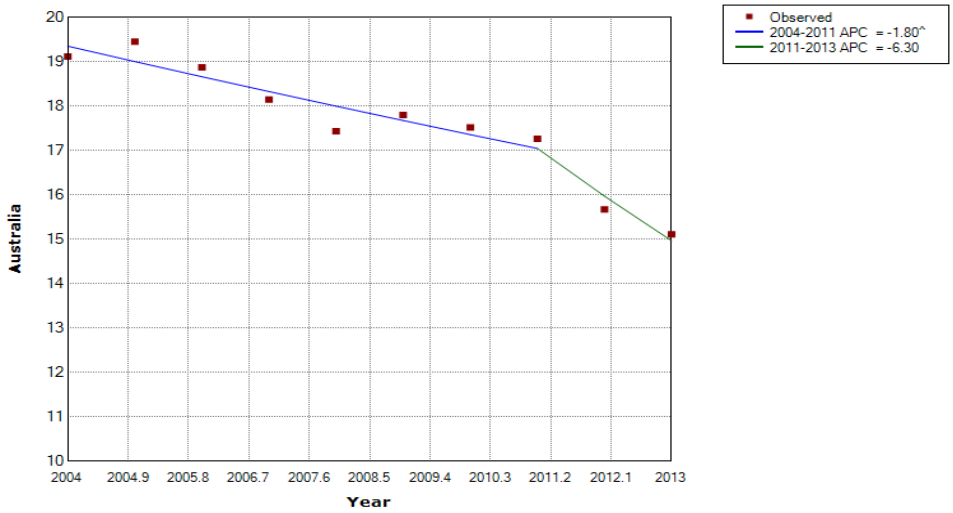

Observed
1998-2002 APC = 9.63^
2002-2007 APC = 0.59
United Kingdom
80
75
70
65
60
55
50
45
40
1998
1998.9
1999.8
2000.7
2001.6
2002.5
2003.4
2004.3
2005.2
2006.1
2007
Year

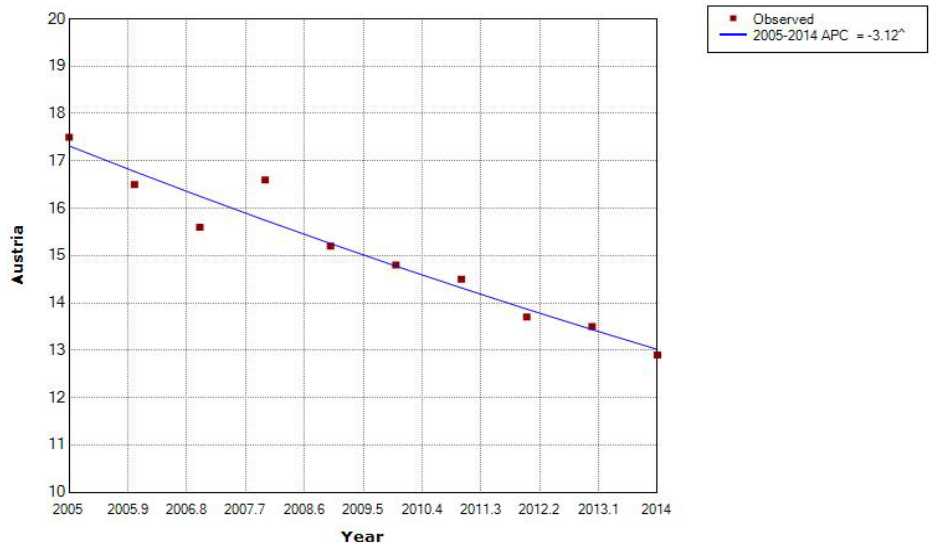

Observed
2004-2009 APC = -0.62
2009-2013 APC = -8.52^
USA Black
290
280
270
260
250
240
230
220
210
200
190
180
170
2004
2004.9
2005.8
2006.7
2007.6
2008.5
2009.4
2010.3
2011.2
2012.1
2013
Year

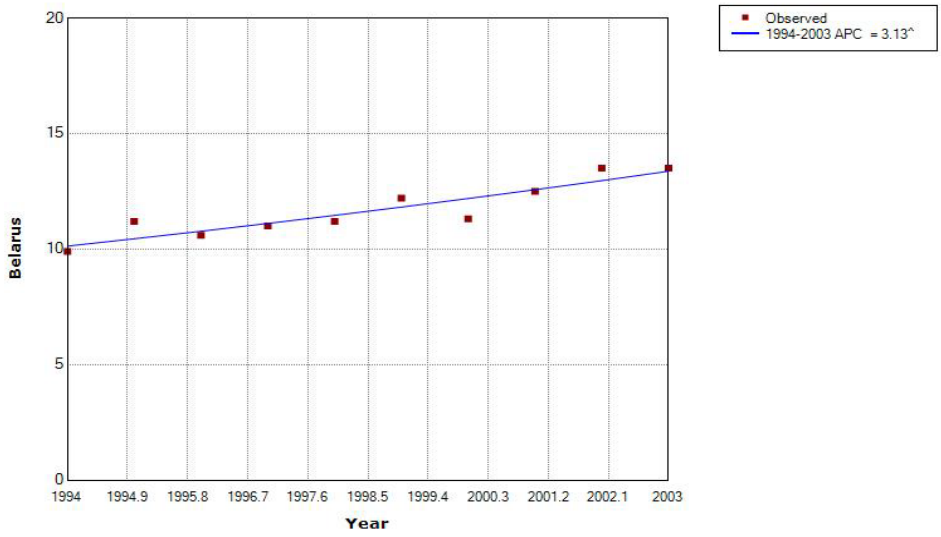

Observed
2004-2009 APC = -0.62
2009-2013 APC = -10.02^
USA White
180
170
160
150
140
130
120
110
100
2004
2004.9
2005.8
2006.7
2007.6
2008.5
2009.4
2010.3
2011.2
2012.1
2013
Year

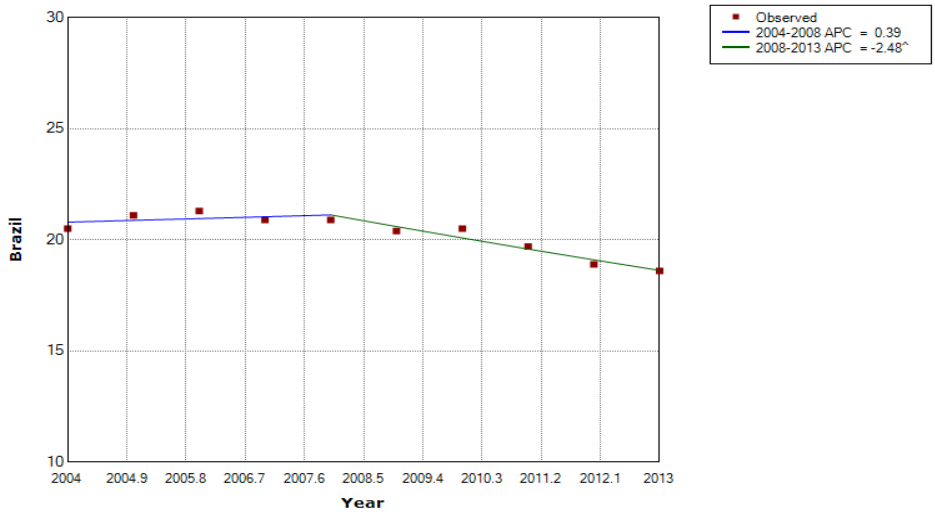

Observed
2004-2009 APC = -0.49
2009-2013 APC = -9.56^
USA
190
180
170
160
150
140
130
120
110
100
2004
2004.9
2005.8
2006.7
2007.6
2008.5
2009.4
2010.3
2011.2
2012.1
2013
Year

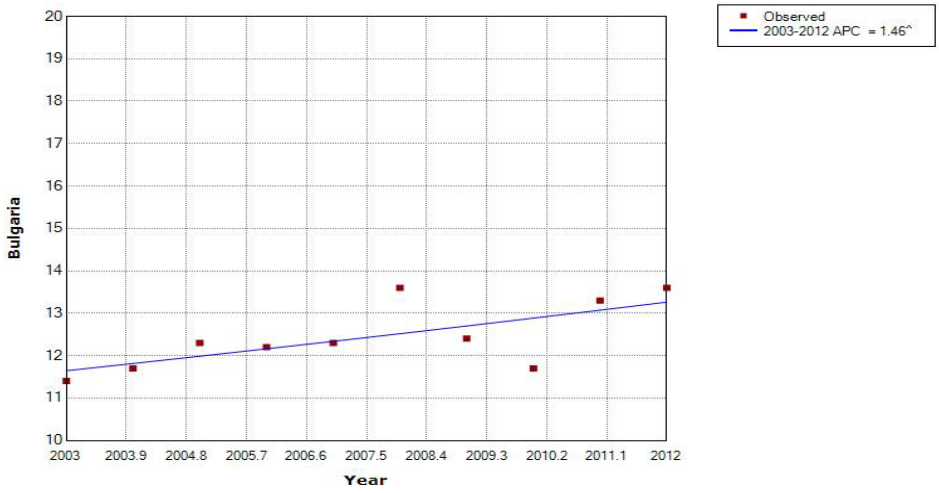
(B) Mortality

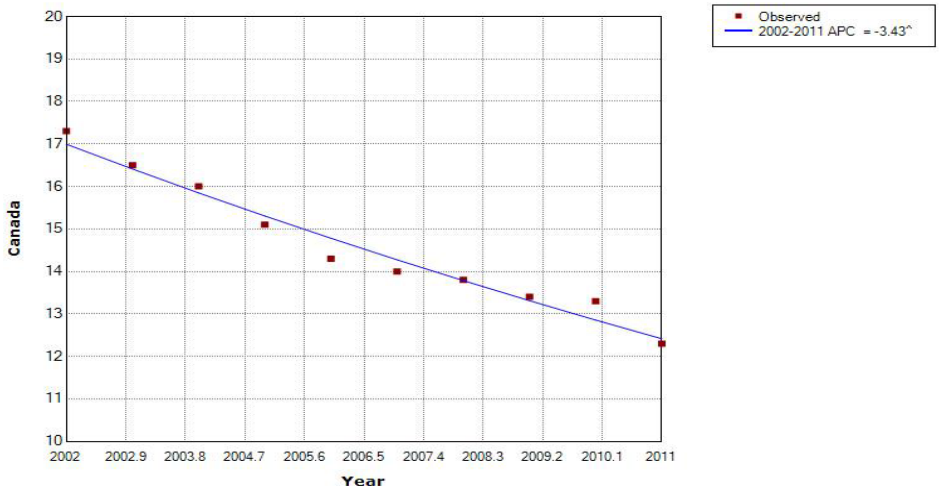

Observed
2004-2011 APC = -1.80^
2011-2013 APC = -6.30
Australia
20
19
18
17
16
15
14
13
12
11
10
2004
2004.9
2005.8
2006.7
2007.6
2008.5
2009.4
2010.3
2011.2
2012.1
2013
Year

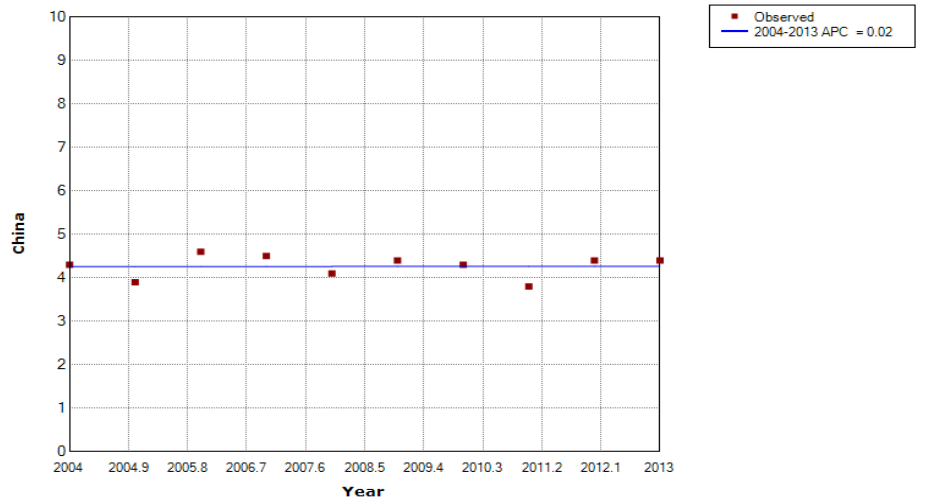

Observed
2005-2014 APC = -3.12^
Austria
Year
20
19
18
17
16
15
14
13
12
11
10
2005
2005.9
2006.8
2007.7
2008.6
2009.5
2010.4
2011.3
2012.2
2013.1
2014

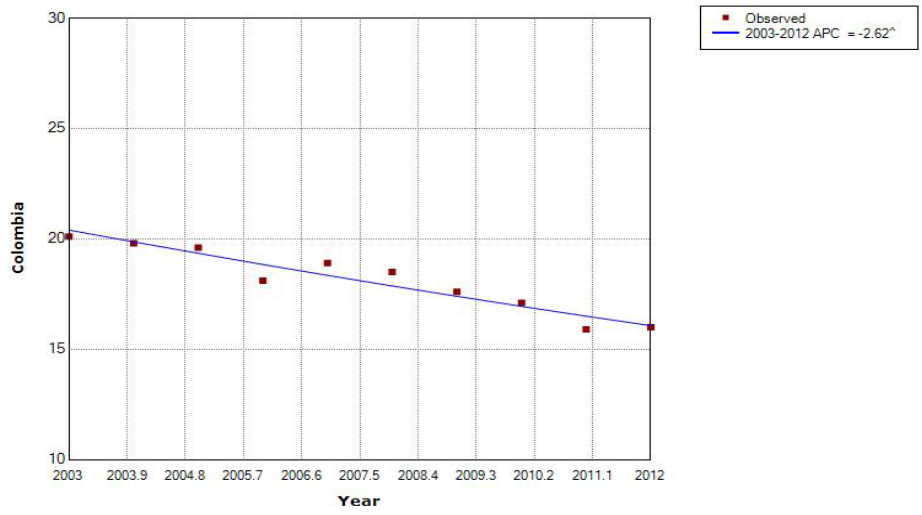

Observed
1994-2003 APC = 3.13^
Belarus
Year
20
15
10
5
0
1994
1994.9
1995.8
1996.7
1997.6
1998.5
1999.4
2000.3
2001.2
2002.1
2003

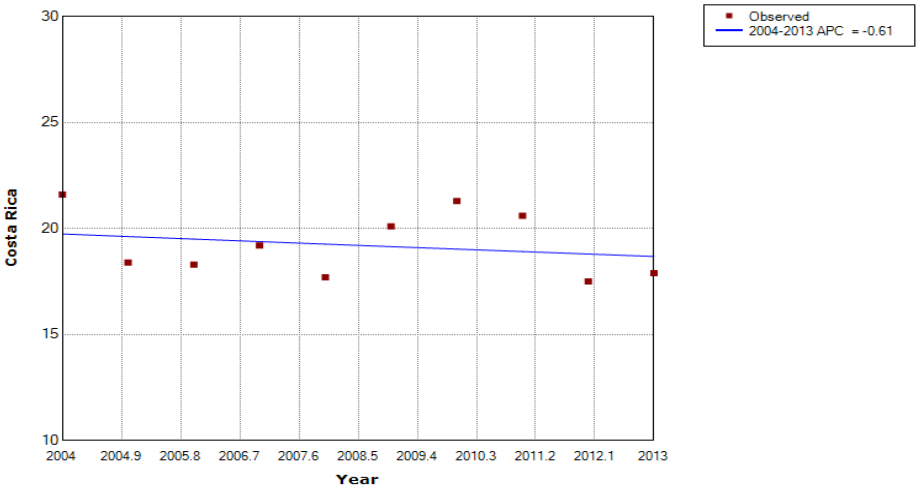

Observed
2004-2008 APC = 0.39
2008-2013 APC = -2.48^
Brazil
Year
30
25
20
15
10
2004
2004.9
2005.8
2006.7
2007.6
2008.5
2009.4
2010.3
2011.2
2012.1
2013

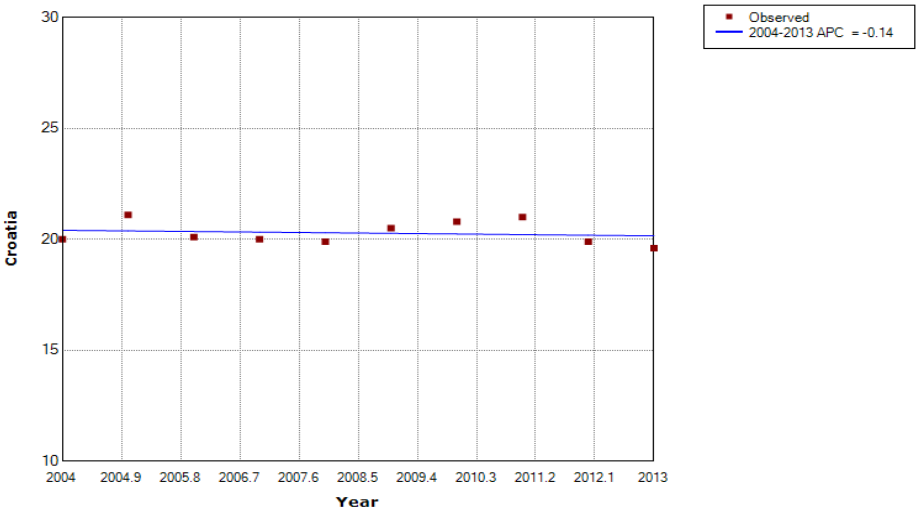

Observed
2003-2012 APC = 1.46^
Bulgaria
Year
20
19
18
17
16
15
14
13
12
11
10
2003
2003.9
2004.8
2005.7
2006.6
2007.5
2008.4
2009.3
2010.2
2011.1
2012

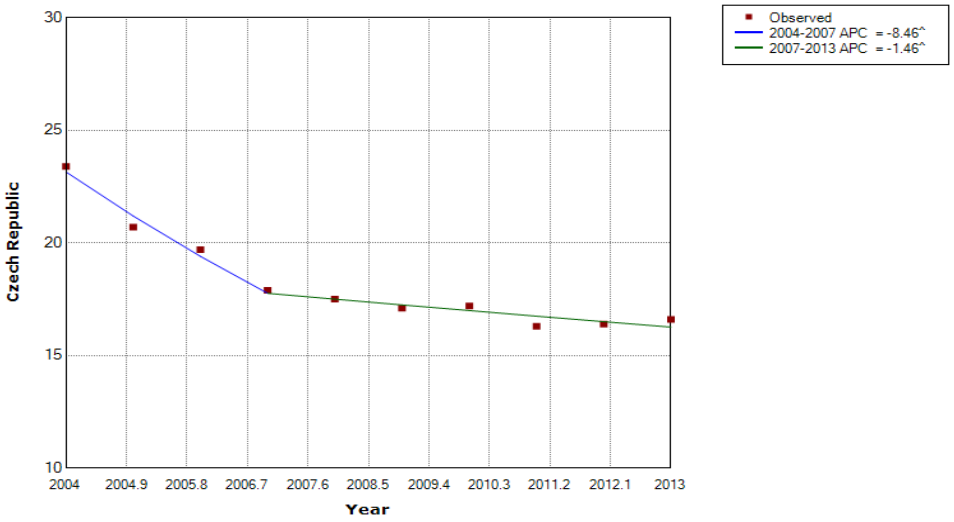

Observed
2002-2011 APC = -3.43^
Canada
Year
20
19
18
17
16
15
14
13
12
11
10
2002
2002.9
2003.8
2004.7
2005.6
2006.5
2007.4
2008.3
2009.2
2010.1
2011

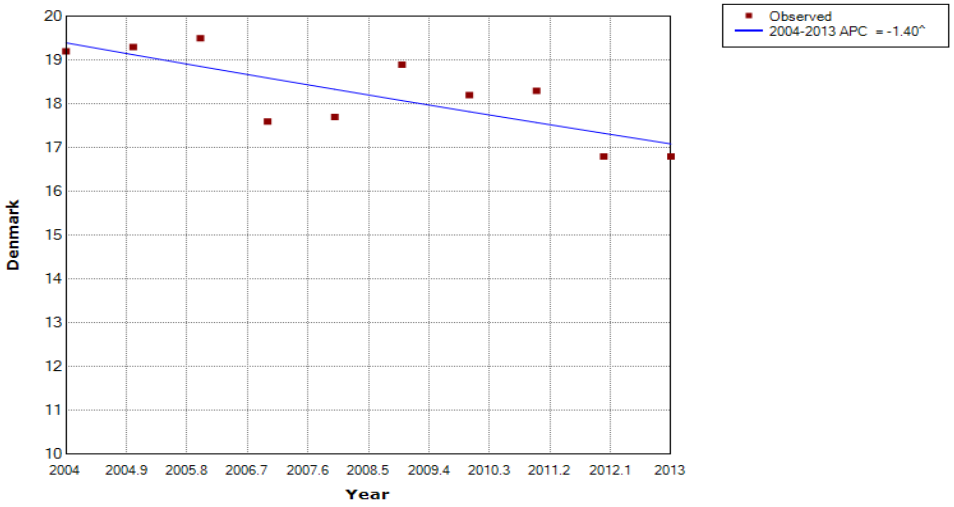

Observed
2004-2013 APC = 0.02
China
Year
10
9
8
7
6
5
4
3
2
1
0
2004
2004.9
2005.8
2006.7
2007.6
2008.5
2009.4
2010.3
2011.2
2012.1
2013

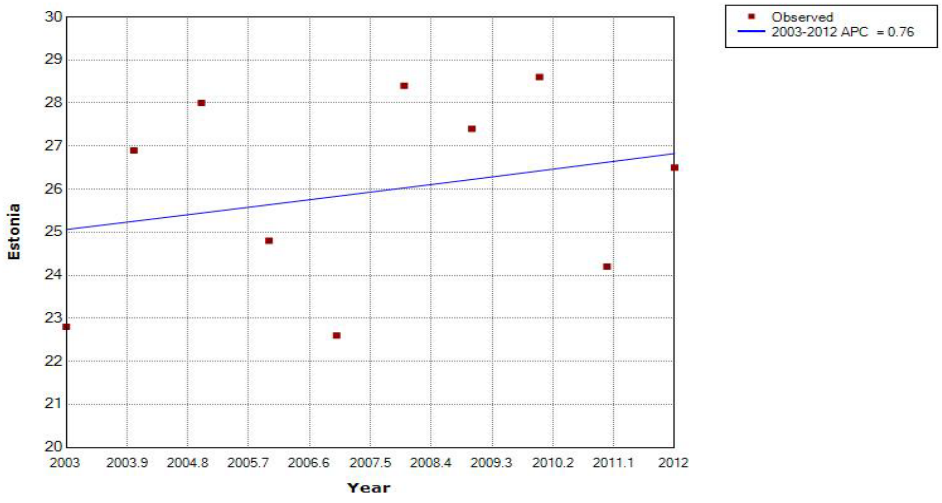

Observed
2003-2012 APC = -2.62^
Colombia
30
25
20
15
10
2003
2003.9
2004.8
2005.7
2006.6
2007.5
2008.4
2009.3
2010.2
2011.1
2012
Year

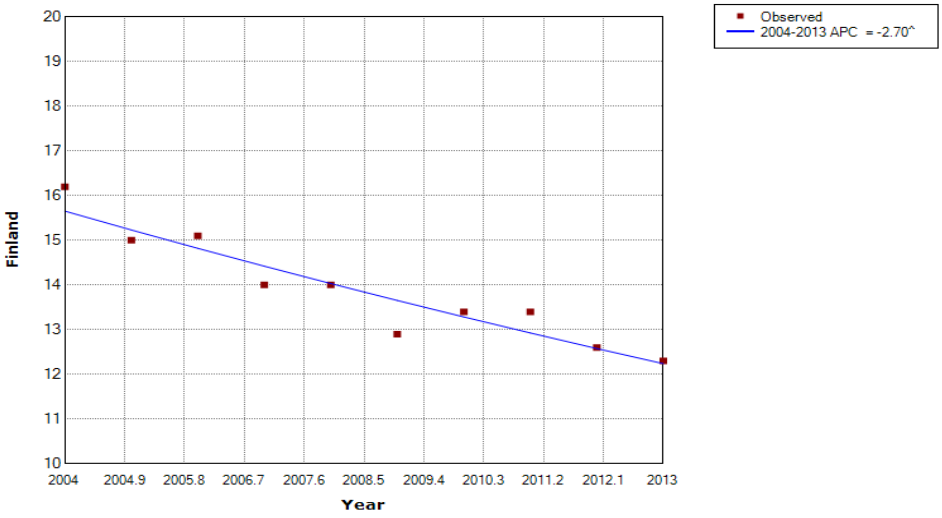

Observed
2004-2013 APC = -0.61
Costa Rica
30
25
20
15
10
2004
2004.9
2005.8
2006.7
2007.6
2008.5
2009.4
2010.3
2011.2
2012.1
2013
Year

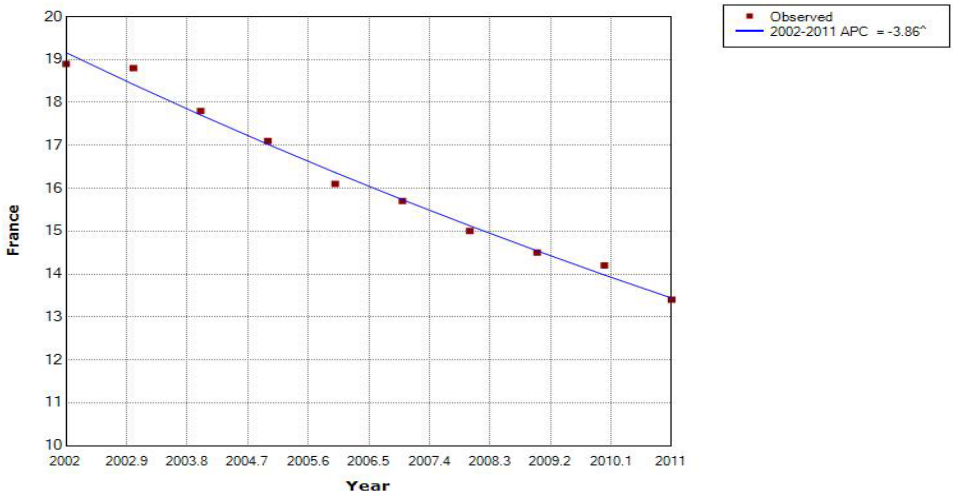

Observed
2004-2013 APC = -0.14
Croatia
30
25
20
15
10
2004
2004.9
2005.8
2006.7
2007.6
2008.5
2009.4
2010.3
2011.2
2012.1
2013
Year

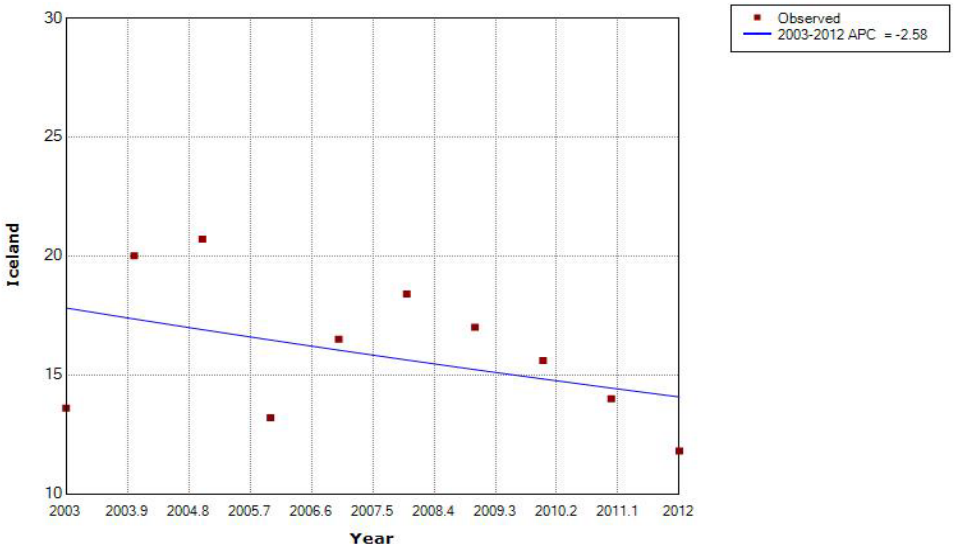

Observed
2004-2007 APC = -8.46^
2007-2013 APC = -1.46^
Czech Republic
30
25
20
15
10
2004
2004.9
2005.8
2006.7
2007.6
2008.5
2009.4
2010.3
2011.2
2012.1
2013
Year

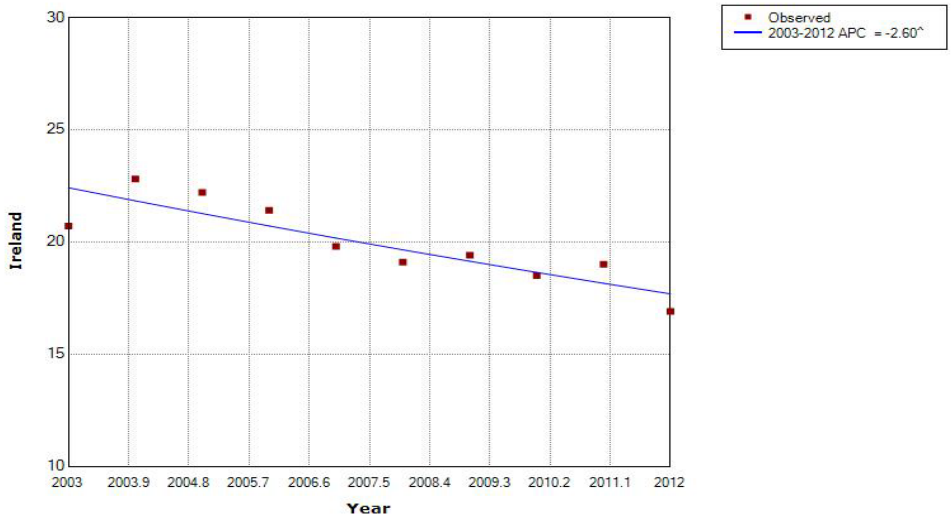

Observed
2004-2013 APC = -1.40^
Denmark
20
19
18
17
16
15
14
13
12
11
10
2004
2004.9
2005.8
2006.7
2007.6
2008.5
2009.4
2010.3
2011.2
2012.1
2013
Year

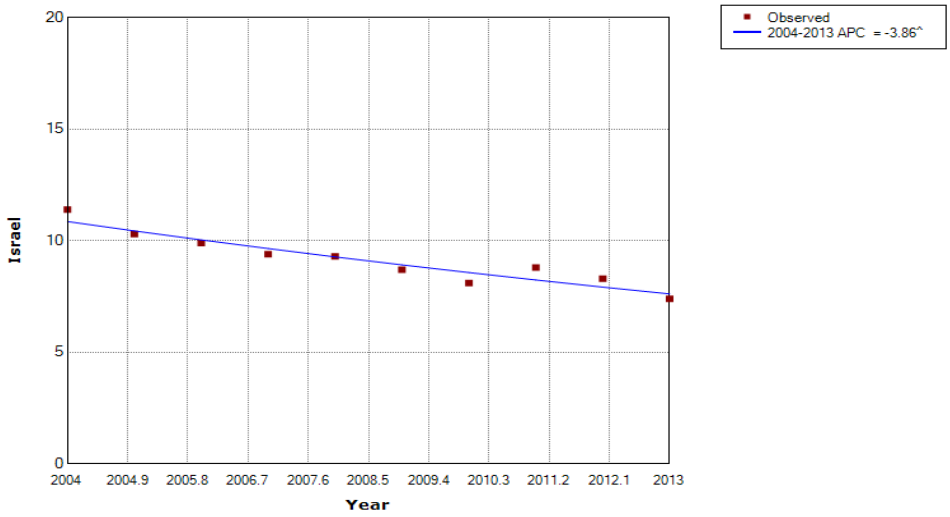

Observed
2003-2012 APC = 0.76
Estonia
30
29
28
27
26
25
24
23
22
21
20
2003
2003.9
2004.8
2005.7
2006.6
2007.5
2008.4
2009.3
2010.2
2011.1
2012
Year

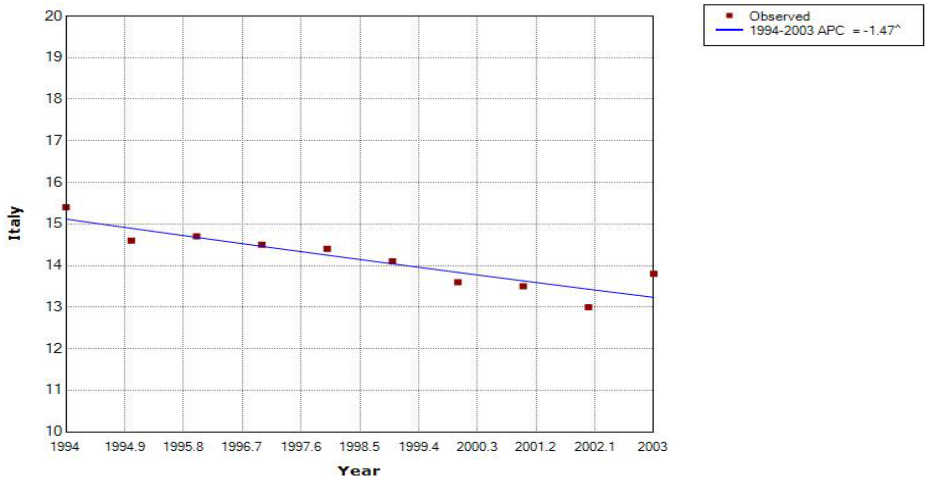

Observed
2004-2013 APC = -2.70^
Finland
Year
20
19
18
17
16
15
14
13
12
11
10
2004
2004.9
2005.8
2006.7
2007.6
2008.5
2009.4
2010.3
2011.2
2012.1
2013

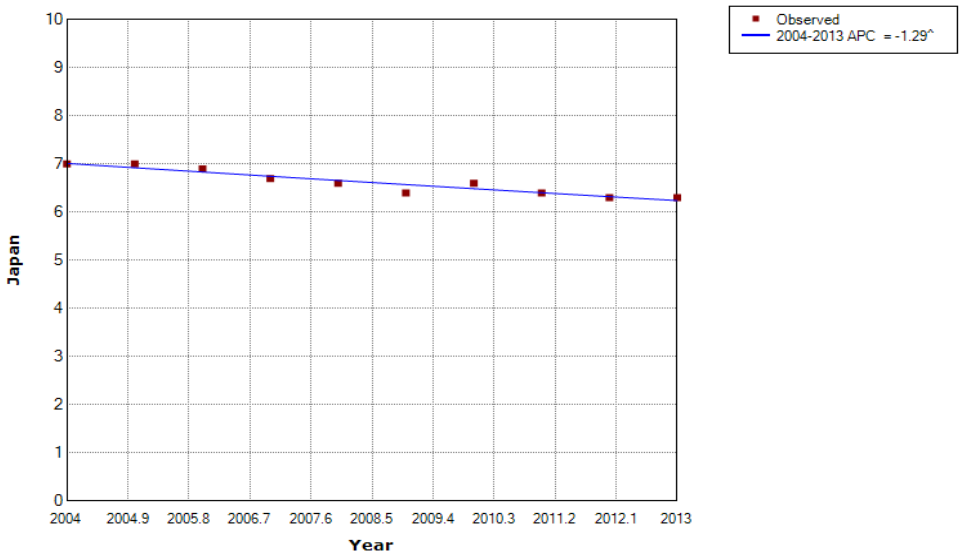

Observed
2002-2011 APC = -3.86^
France
Year
20
19
18
17
16
15
14
13
12
11
10
2002
2002.9
2003.8
2004.7
2005.6
2006.5
2007.4
2008.3
2009.2
2010.1
2011

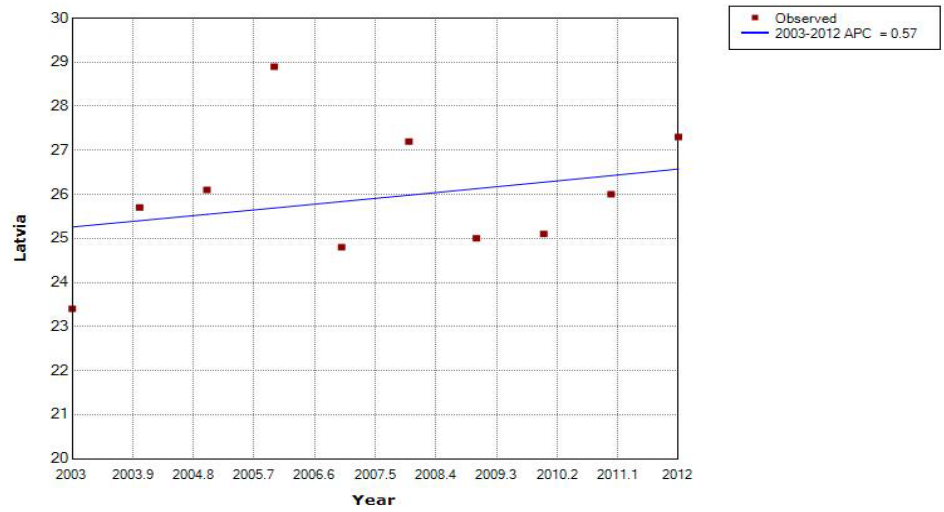

Observed
2003-2012 APC = -2.58
Iceland
Year
30
25
20
15
10
2003
2003.9
2004.8
2005.7
2006.6
2007.5
2008.4
2009.3
2010.2
2011.1
2012

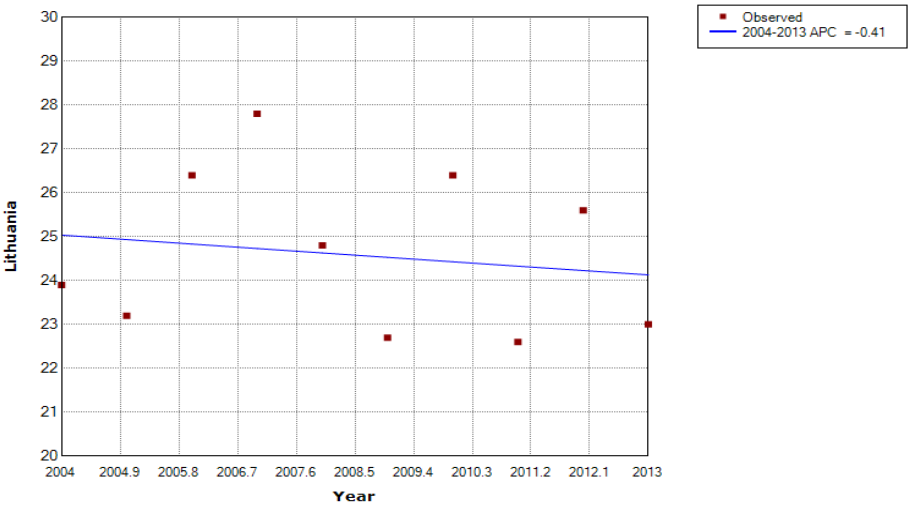

Observed
2003-2012 APC = -2.60^
Ireland
30
25
20
15
10
2003
2003.9
2004.8
2005.7
2006.6
2007.5
2008.4
2009.3
2010.2
2011.1
2012
Year

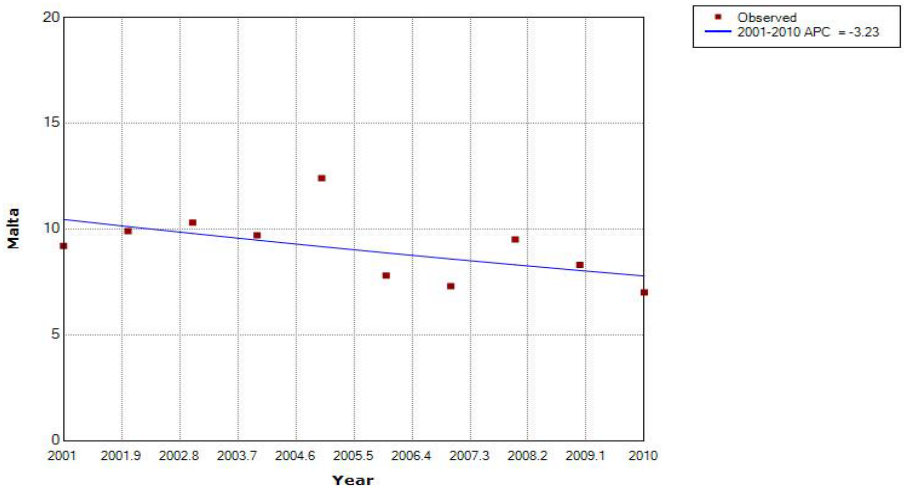

Observed
2004-2013 APC = -3.86^
Israel
20
15
10
5
0
2004
2004.9
2005.8
2006.7
2007.6
2008.5
2009.4
2010.3
2011.2
2012.1
2013
Year

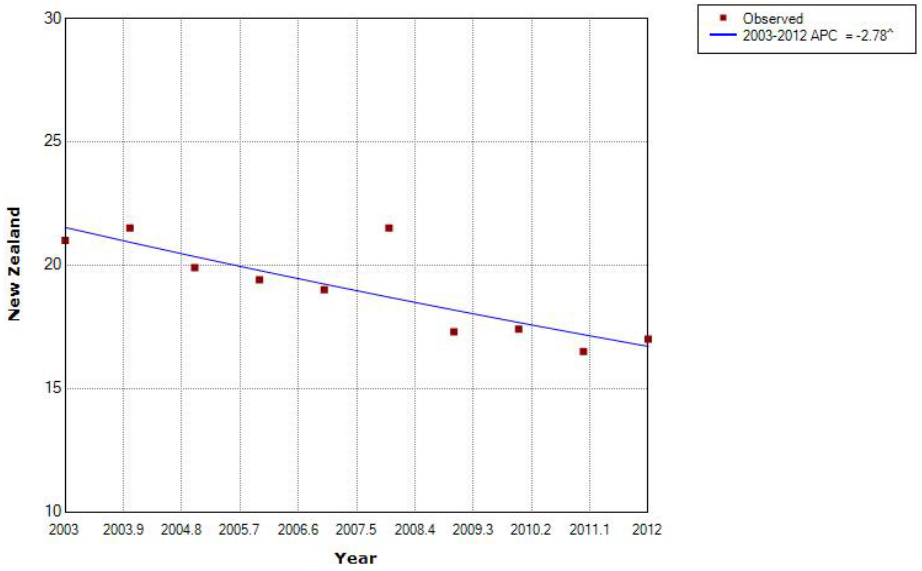

Observed
1994-2003 APC = -1.47^
Italy
20
19
18
17
16
15
14
13
12
11
10
1994
1994.9
1995.8
1996.7
1997.6
1998.5
1999.4
2000.3
2001.2
2002.1
2003
Year

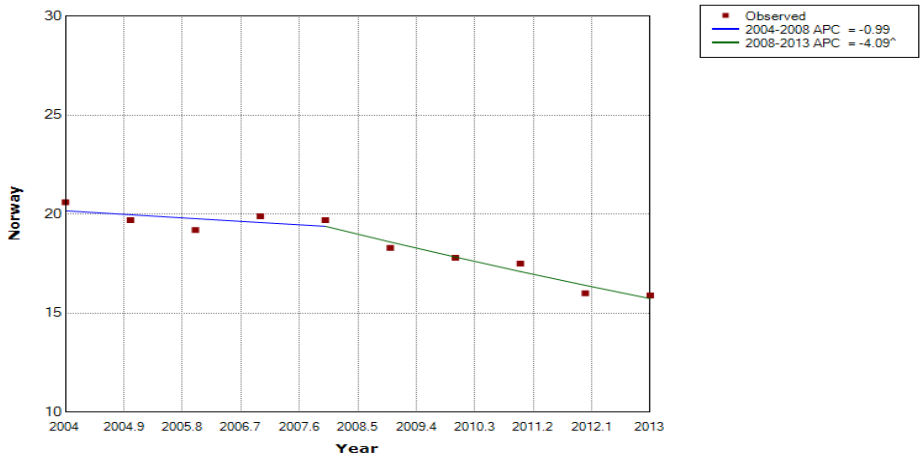

Observed
2004-2013 APC = -1.29^
Japan
Year
0
1
2
3
4
5
6
7
8
9
10
2004
2004.9
2005.8
2006.7
2007.6
2008.5
2009.4
2010.3
2011.2
2012.1
2013

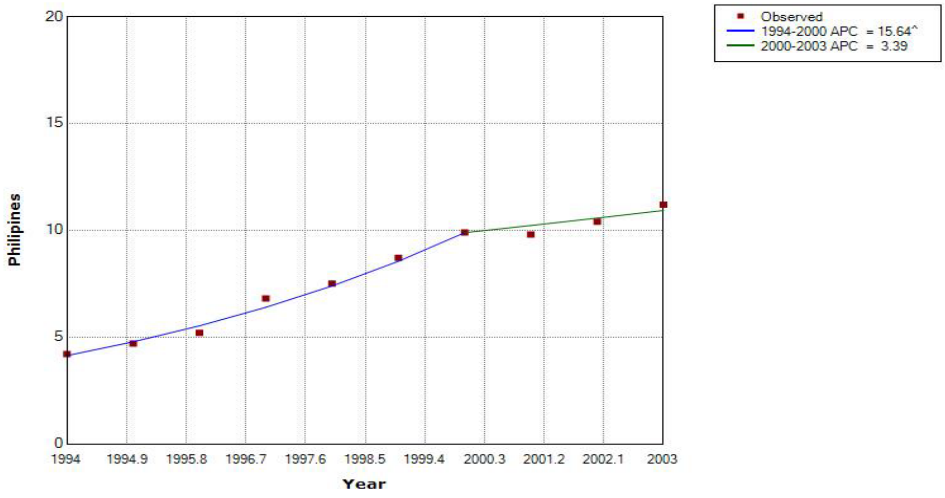

Observed
2003-2012 APC = 0.57
Latvia
Year
20
21
22
23
24
25
26
27
28
29
30
2003
2003.9
2004.8
2005.7
2006.6
2007.5
2008.4
2009.3
2010.2
2011.1
2012

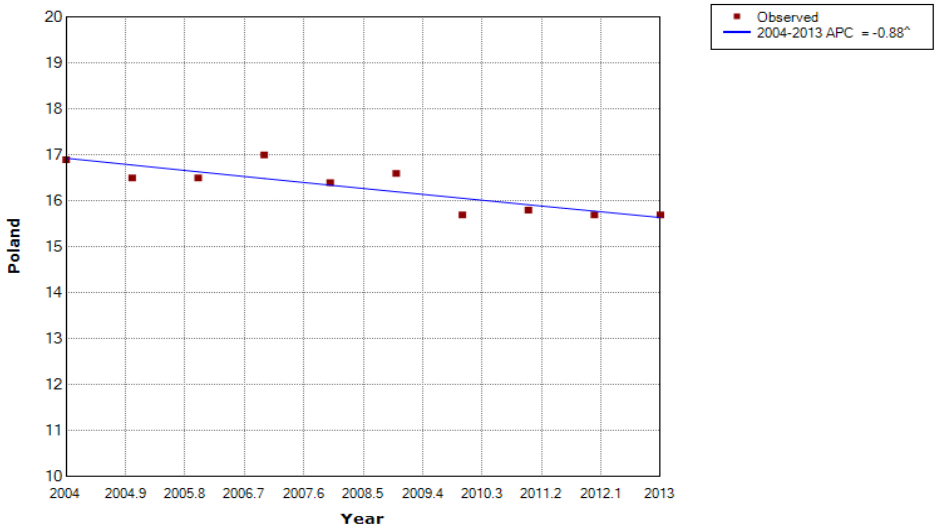

Observed
2004-2013 APC = -0.41
Lithuania
Year
20
21
22
23
24
25
26
27
28
29
30
2004
2004.9
2005.8
2006.7
2007.6
2008.5
2009.4
2010.3
2011.2
2012.1
2013

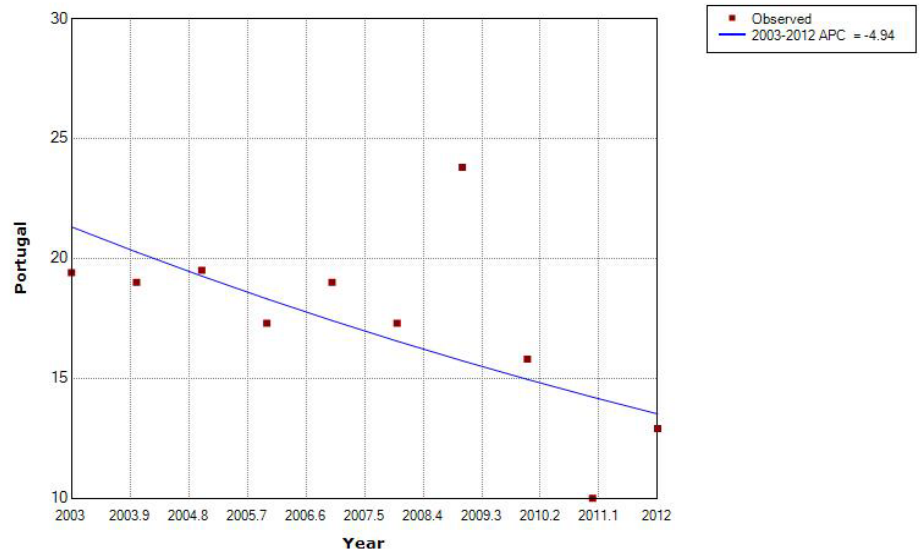

Observed
2001-2010 APC = -3.23
Malta
20
15
10
5
0
2001
2001.9
2002.8
2003.7
2004.6
2005.5
2006.4
2007.3
2008.2
2009.1
2010
Year

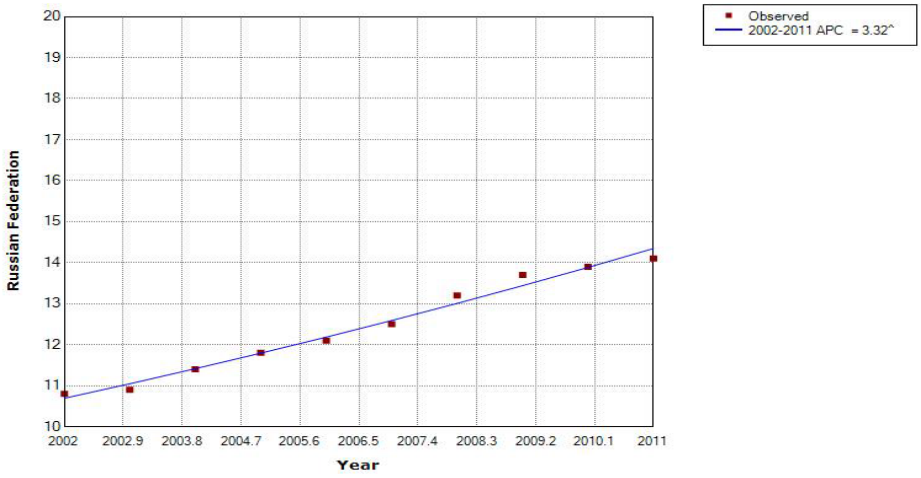

Observed
2003-2012 APC = -2.78^
New Zealand
30
25
20
15
10
2003
2003.9
2004.8
2005.7
2006.6
2007.5
2008.4
2009.3
2010.2
2011.1
2012
Year

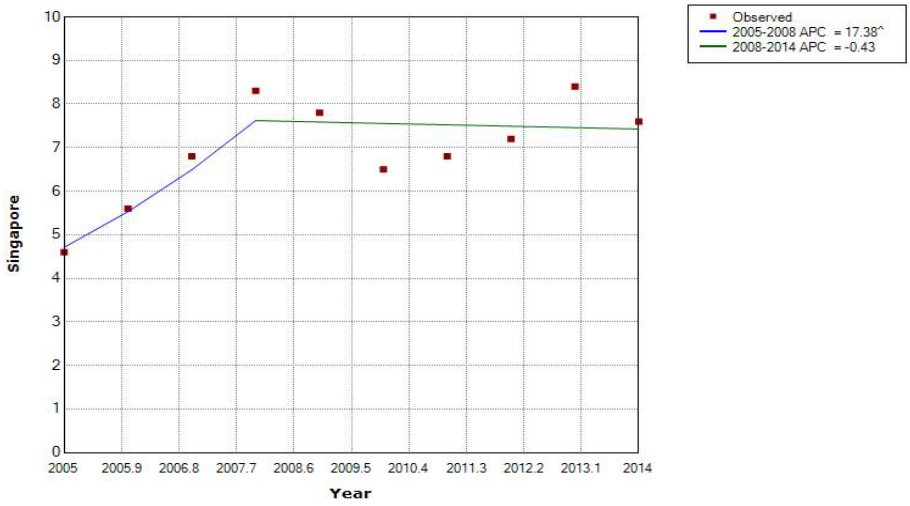

Observed
2004-2008 APC = -0.99
2008-2013 APC = -4.09^
Norway
30
25
20
15
10
2004
2004.9
2005.8
2006.7
2007.6
2008.5
2009.4
2010.3
2011.2
2012.1
2013
Year

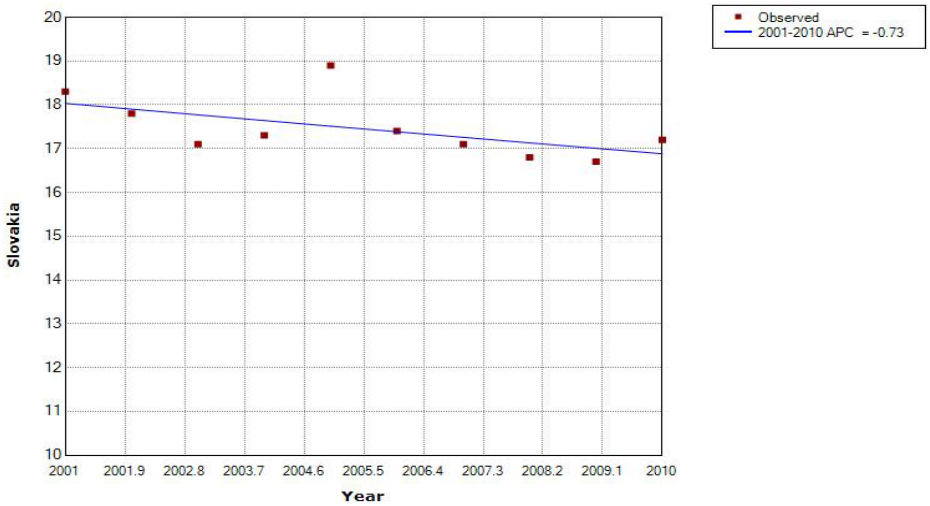

Observed
1994-2000 APC = 15.64^
2000-2003 APC = 3.39
Philipines
Year
0
5
10
15
20
1994
1994.9
1995.8
1996.7
1997.6
1998.5
1999.4
2000.3
2001.2
2002.1
2003

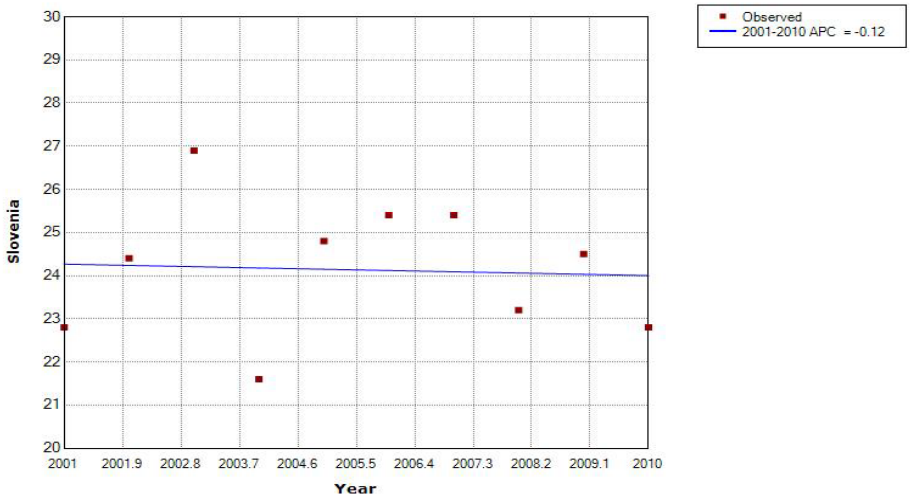

Observed
2004-2013 APC = -0.88^
Poland
Year
10
11
12
13
14
15
16
17
18
19
20
2004
2004.9
2005.8
2006.7
2007.6
2008.5
2009.4
2010.3
2011.2
2012.1
2013

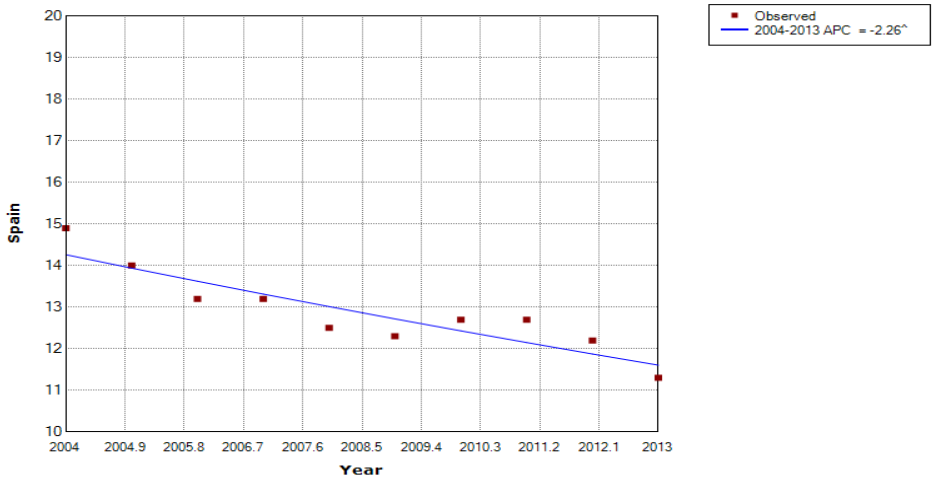

Observed
2003-2012 APC = -4.94
Portugal
Year
10
15
20
25
30
2003
2003.9
2004.8
2005.7
2006.6
2007.5
2008.4
2009.3
2010.2
2011.1
2012

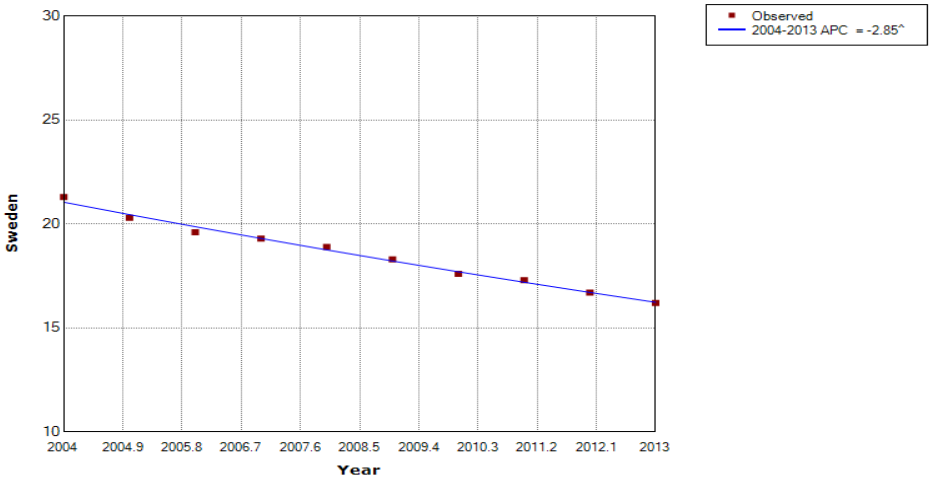

Observed
2002-2011 APC = 3.32^
Russian Federation
Year
20
19
18
17
16
15
14
13
12
11
10
2002
2002.9
2003.8
2004.7
2005.6
2006.5
2007.4
2008.3
2009.2
2010.1
2011

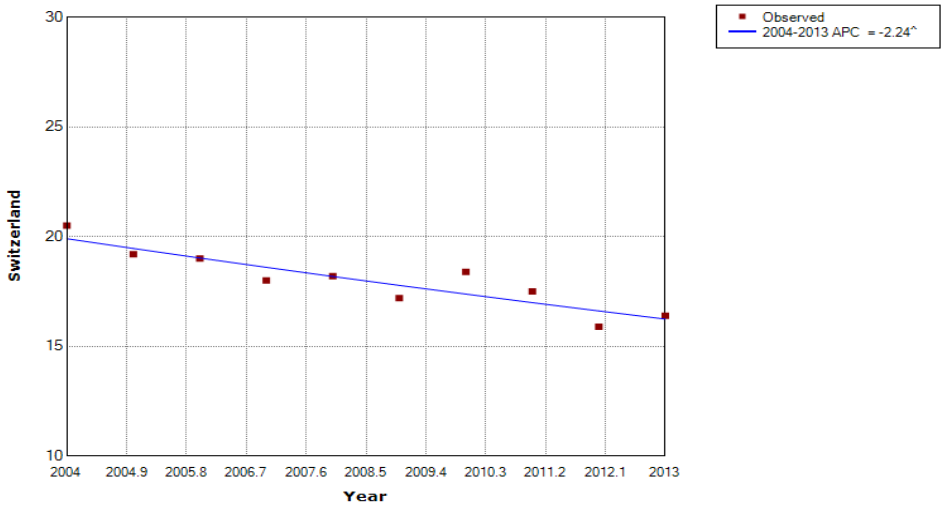

Observed
2005-2008 APC = 17.38^
2008-2014 APC = -0.43
Singapore
Year
10
9
8
7
6
5
4
3
2
1
0
2005
2005.9
2006.8
2007.7
2008.6
2009.5
2010.4
2011.3
2012.2
2013.1
2014

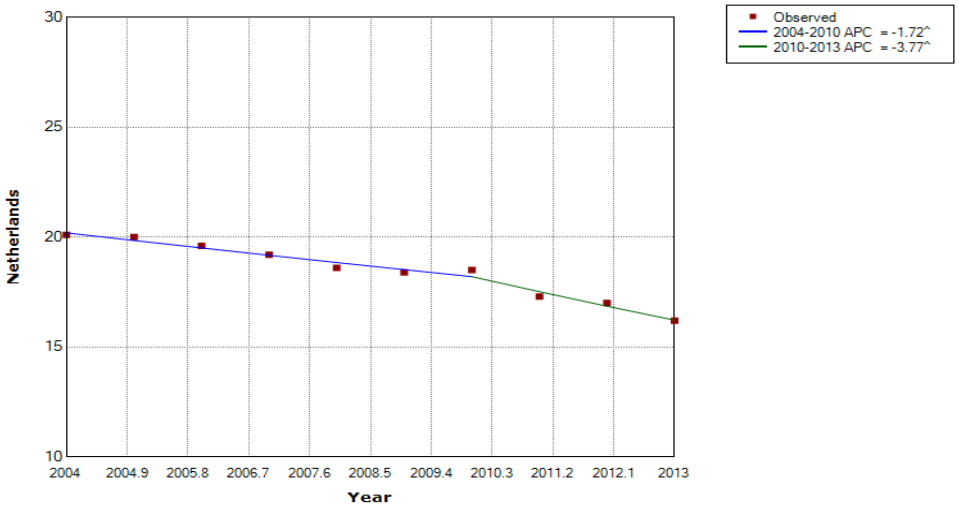

Observed
2001-2010 APC = -0.73
Slovakia
Year
20
19
18
17
16
15
14
13
12
11
10
2001
2001.9
2002.8
2003.7
2004.6
2005.5
2006.4
2007.3
2008.2
2009.1
2010

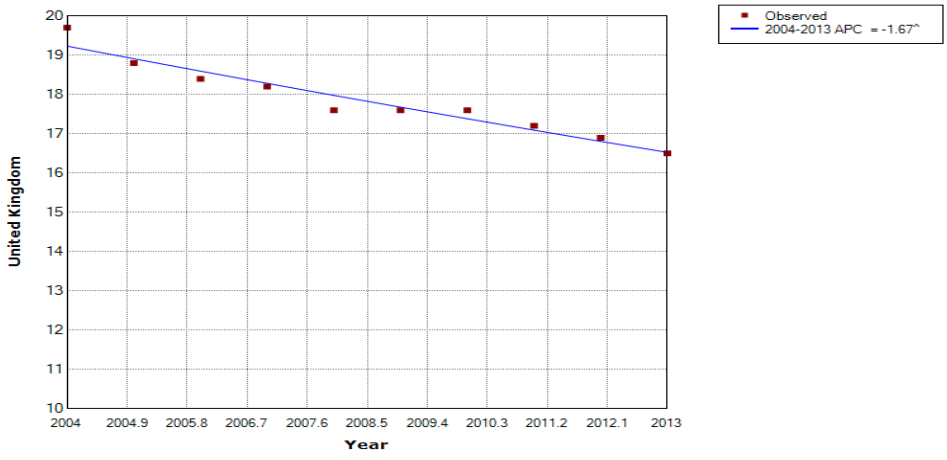

Observed
2001-2010 APC = -0.12
Slovenia
30
29
28
27
26
25
24
23
22
21
20
2001
2001.9
2002.8
2003.7
2004.6
2005.5
2006.4
2007.3
2008.2
2009.1
2010
Year

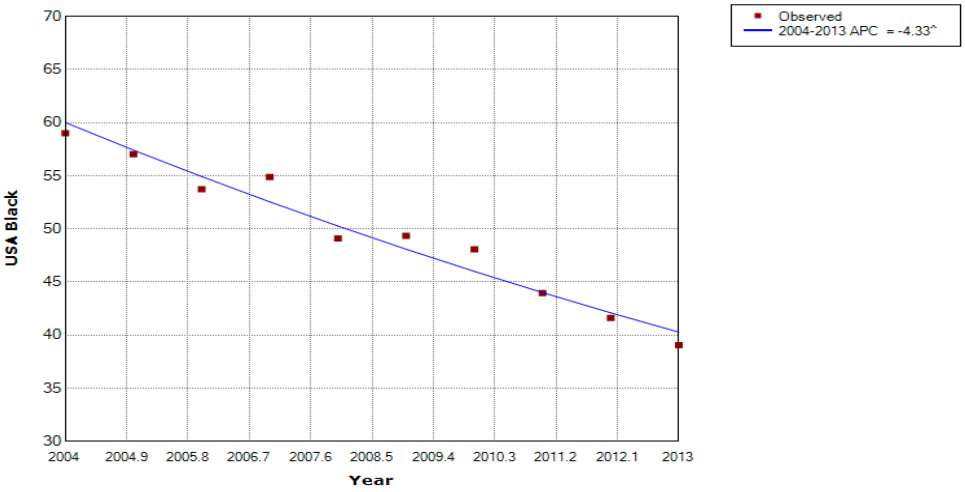

Observed
2004-2013 APC = -2.26^
Spain
20
19
18
17
16
15
14
13
12
11
10
2004
2004.9
2005.8
2006.7
2007.6
2008.5
2009.4
2010.3
2011.2
2012.1
2013
Year

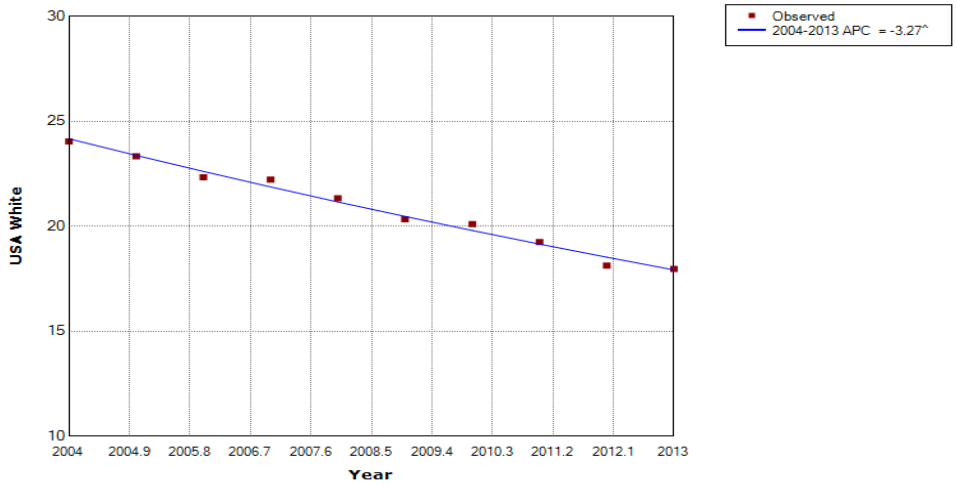

Observed
2004-2013 APC = -2.85^
Sweden
30
25
20
15
10
2004
2004.9
2005.8
2006.7
2007.6
2008.5
2009.4
2010.3
2011.2
2012.1
2013
Year


Observed
2004-2013 APC = -2.24^
Switzerland
30
25
20
15
10
2004
2004.9
2005.8
2006.7
2007.6
2008.5
2009.4
2010.3
2011.2
2012.1
2013
Year


Observed
2004-2010 APC = -1.72^
2010-2013 APC = -3.77^
Netherlands
30
25
20
15
10
2004
2004.9
2005.8
2006.7
2007.6
2008.5
2009.4
2010.3
2011.2
2012.1
2013
Year


Observed
2004-2013 APC = -1.67^
United Kingdom
20
19
18
17
16
15
14
13
12
11
10
2004
2004.9
2005.8
2006.7
2007.6
2008.5
2009.4
2010.3
2011.2
2012.1
2013
Year





0 Joinpoints