Int. J. Cancer: **123,** 421–429 (2008)

Recent trends in prostate cancer mortality show a continuous decrease in several countries

Christine Bouchardy[1], Gerald Fioretta[1], Elisabetta Rapiti[1], Helena Maria Verkooijen[1,2], Charles Henry Rapin[3], France Schmidlin[4], Raymond Miralbell[5] and Roberto Zanetti[1,6]*

[1]*Geneva Cancer Registry, Institute for Social and Preventive Medicine, University of Geneva, Geneva, Switzerland*
[2]*Department of Community Occupational and Family Medicine, National University of Singapore, Singapore*
[3]*Association PROSCA, Geneva, Switzerland*
[4]*Service of Urology, Geneva University Hospitals, Geneva, Switzerland*
[5]*Service of Radio-oncology, Geneva University Hospitals, Geneva, Switzerland*
[6]*Piedmont Cancer Registry, CPO, Torino, Italy*

Prostate specific antigen (PSA) screening was introduced to detect prostate cancer at an early stage and to reduce prostate cancer-specific mortality. Until results from clinical trials are available, the efficacy of PSA screening in reducing prostate cancer mortality can be estimated by surveillance of prostate cancer mortality trends. Our study analyzes recent trends in prostate cancer mortality in 38 countries. We used the IARC-WHO cancer mortality database and performed joinpoint analysis to examine prostate cancer mortality trends and identified 3 patterns. In USA, and to a lesser extent in Germany, Switzerland, Canada, France, Italy and Spain, prostate cancer-specific mortality decreased to a level lower than before the introduction of PSA screening. In Australia, New Zealand, Austria, Finland, The Netherlands, Norway, United Kingdom, Hungary, Slovakia, Israel, Singapore, Sweden and Portugal, mortality from prostate cancer decreased but rates remain higher than before the introduction of PSA screening. Prostate cancer mortality continued to increase in Belgium, Denmark, Greece, Ireland, Bulgaria, Czech Republic, Belarus, Ukraine, Russian Federation, Romania, Poland, Argentina, Chile, Cuba, Mexico, Japan, China Hong Kong and the Republic of Korea. The trends in prostate cancer mortality rates in examined countries suggest that PSA screening may be effective in reducing mortality from prostate cancer.

Key words: prostate cancer; mortality; time trends; PSA

Prostate specific antigen (PSA) screening aims to detect early stage prostate cancer, allowing curative treatment and consequently to reduce prostate cancer-specific mortality at a population level. The effectiveness of PSA screening remains under debate. Randomised trials are ongoing in the USA and Europe to provide formal evidence that PSA screening can significantly reduce prostate cancer-specific mortality, and to define the best screening strategy.[1] The US trial (part of the prostate, lung, colorectal and ovarian cancer—PLCO screening trial) has enrolled 38,350 men in the screening arm.[2,3] The European Randomised Study of Screening for Prostate Cancer recruited 183,000 subjects in 8 European countries.[1,4,5] The latter trial also evaluates adverse effects of PSA screening, including false positive or negative results, overdiagnosis and overtreatment of localised, low grade disease. The final results of these trials are expected in 2008–2010.[5]

Since its introduction in the late 1980s, PSA screening is rapidly spreading, particularly in the USA. According to the National Health Interview Survey 2000, over 50% of men aged >65 years had a PSA test in the previous year.[6] In Europe, PSA screening was introduced later and the rates of opportunistic screening are lower than in the USA.[4,5,7,8] In recent years, many changes in prostate cancer treatment have occurred, including new surgical approaches for localised disease, improved irradiation techniques and antiandrogenic therapy. Only clinical trials can distinguish between the respective contributions of screening or therapeutic progress to the decrease in mortality. But from a general public health point of view, to observe a decrease in mortality, even before the availability of experimental evidence, might suggest that things are going in the right direction. Until conclusive scientific results on the efficacy of PSA screening are reached, trends in prostate cancer mortality can help to evaluate the impact of screening.

Moreover, in the case of prostate cancer, mortality data have became nowadays the only unbiased current descriptive statistics. Incidence rates, inflated by a large proportion of preclinical diagnoses due to PSA, have reached levels higher than 200 cases/100,000/year is some USA populations and higher than 150 in some European ones (crude rates).[9] Those rates are the sum of the true incidence and of the anticipation of cases. For the same reason, population based survival statistics are biased by a large proportion of anticipated diagnoses (lead time bias at population level) showing 5-year survival proportions higher than 90% (observed survival) in some European countries.[10] Incidence and survival data seems to have today little or no role for evaluating the effectiveness of PSA practice.

Several systematic analyzes of mortality time trends of prostate cancer were published.[8,11–23] The majority of these studies presented data until 2001, and 2 regional studies (Umbria in Italy and Tyrol in Austria) reported data until 2004.[20,22] Overall, published analyzes reported a significant decrease in mortality rates in the USA, Canada and Austria, followed by the United Kingdom, France, Italy, Germany, and more recently by Australia, and Spain.

The aim of our study is to examine and critically discuss the most recent international trends in prostate cancer mortality.

Material and methods

Data sources, country selection and period

We used the World Health Organisation mortality data provided from the International Agency for Research on Cancer (IARC-WHO).[24] This database, updated in 2006, contains cancer mortality statistics for selected sites and countries. For prostate cancer mortality, data are available for 49 countries, in Europe, North America and Oceania, as well as some populations in Central and South America, East and Southeast Asia. With the exception of Israel, the database does not include the Middle East and African countries.

We examined the data of all 49 countries. We excluded countries with unstable time trends due to low prostate cancer mortality rates and/or small populations. The remaining 38 countries are listed in Table I.

Grant sponsor: Swiss National Science Foundation PROSPER; Grant number: 3233-069350.
***Correspondence to:** Piedmont Cancer Registry-CPO, Via San Francesco da Paola 31, 10123, Torino, Italy. Fax: +39-011-633-3861.
E-mail: roberto.zanetti@cpo.it
Received 1 August 2007; Accepted after revision 11 January 2008
DOI 10.1002/ijc.23520
Published online 1 May 2008 in Wiley InterScience (www.interscience.wiley.com).

TABLE I – SELECTED COUNTRIES AND PERIOD OF DATA AVAILABILITY, BY CONTINENTAL AREA

Western Europe
Austria (1955–2004)
Belgium (1954–1997)
Denmark (1951–2001)
Finland (1952–2004)
France (1950–2002)
Germany (1973–2004)
Greece (1961–2003)
Ireland (1950–2002)
Italy (1951–2002)
Netherlands (1950–2004)
Norway (1951–2003)
Portugal (1955–2003)
Spain (1951–2003)
Sweden (1951–2002)
Switzerland (1951–2002)
U.K. (1950–2002)
Central and Eastern Europe
Belarus (1981–2003)
Bulgaria (1964–2004)
Czech Republic (1986–2004)
Hungary (1955–2003)
Poland (1959–2003)
Romania (1969–2004)
Russian Federation (1980–2004)
Slovakia (1992–2002)
Ukraine (1981–2004)
Middle East
Israel (1975–2003)
Far East
China, Hong Kong (1960–2002)
Japan (1950–2003)
Republic of Korea (1985–2002)
Singapore (1963–2003)
North America
Canada (1950–2002)
USA (1950–2002)
Central and South America
Argentina (1966–1970; 1977–1996)
Chile (1955–1982; 1984–1994)
Cuba (1970–1996)
Mexico (1958–1973; 1981–1983; 1985–1995)
Oceania
Australia (1950–2002)
New Zealand (1950–2000)

For most countries mortality data were available from the beginning of the 1950s until the years 2002–2004. Some data were missing for Belgium, Argentina, Chile, Cuba and Mexico. Since our aim was to estimate the effect of the PSA screening introduction, we limited our study to the period 1975–2004.

Statistical analyzes

The IARC-WHO mortality database provides age standardised (World Standard Population) mortality rates with their standard errors and computing tools for overall, age-specific and cohort time trend analysis. We conducted joinpoint analyzes of age standardised mortality rates using the Joinpoint Regression Program (version 3.0).[25] This procedure fits a model based on a minimum number of joinpoints (the points in which there is a change in slope) observed in a series of rates over time. Joinpoint regression analyzes assume a log-linear model. This programme starts with a model with zero joinpoints and adds more joinpoints, with a maximum of three, until the new model has a statistically significant difference compared to the previous one. The generation of models and the test of significance were performed using the Monte Carlo Permutation method. We performed this analysis for all 38 countries. For 3 of them (USA, Germany and Switzerland) we also used the computing facilities of the IARC-WHO database to calculate age-specific and cohort mortality time trends.

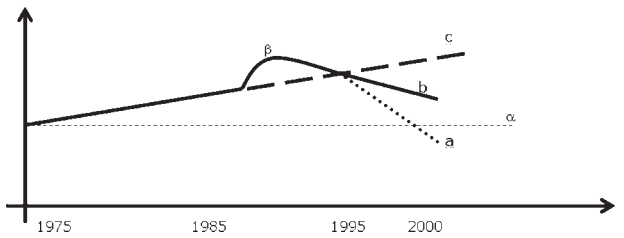

FIGURE 1 – Prostate cancer mortality interpretating scheme: (a) decrease till a level lower than before the PSA era; (b) decrease, but with the recent level still over the previous one; (c) the mortality still increases; (α) baseline; and (β) momentary "hump."

Choosing the patterns for data interpreting

After performing the analysis, we grouped the results according to 3 different general patterns (Fig. 1). Pattern (a) shows a decline in prostate cancer mortality to a level lower than before the PSA era; pattern (b) shows a decrease not yet below the pre-PSA era level; and pattern (c) corresponds to a continuous increase in prostate cancer mortality.

Our analysis of mortality data is a classical descriptive one, and formal statistical analysis (joinpoint regression) was used only for analysing the time trend. The patterns were chosen *a posteriori* as a simple organization for reading the results, without formal testing. The 3 patterns correspond to a public health perspective: non yet a gain in mortality (*i*), yet a tendency (*ii*) or not yet a tendency (*iii*) toward a control of prostate cancer mortality.

Figure 1 also includes a baseline (α) as reference level, and a momentary hump (β) in mortality that can be observed for some countries after the generalisation of the PSA test.

Results

Among the 38 countries included in our study, 7 populations showed a mortality decrease to a level lower than before the introduction of PSA screening, 13 countries showed a mortality decrease with mortality rates still higher than before the introduction of PSA screening, and 18 showed a mortality increase.

Pattern a: Mortality decreased to a level lower than before the introduction of PSA screening

USA, Canada, France, Germany, Spain, Italy and Switzerland presented similar patterns: a rise and fall of prostate cancer mortality, with lower levels in recent years compared to the mid-1970s (Fig. 2, pattern (a). In the USA, Germany and Switzerland the recent level was well below the initial one, and the decreasing trends started in the mid-1990s. In Spain too, the fall in mortality reached a level clearly below the previous one, but it started later. Canada had a pattern similar to the USA both in terms of period and slope, but the mortality reduction was still smaller. In France and Italy, recent mortality rates were slightly below the level of the 1970s, but the mortality decrease started before the PSA era.

Pattern b: Mortality decreased with mortality rates still higher than before the introduction of PSA screening

In Australia, New Zealand, Austria, Finland, The Netherlands, Norway, United Kingdom, Hungary, Slovakia, Israel, Singapore, Sweden and Portugal after a temporary rise, prostate cancer mortality declined at the end of the 1990s. However, the most recent mortality rates were still higher than in the pre-PSA era (Fig. 2, pattern b). For most countries in this group the patterns were relatively similar to that of the previous group but delayed in time, as the falling trend started some years later.

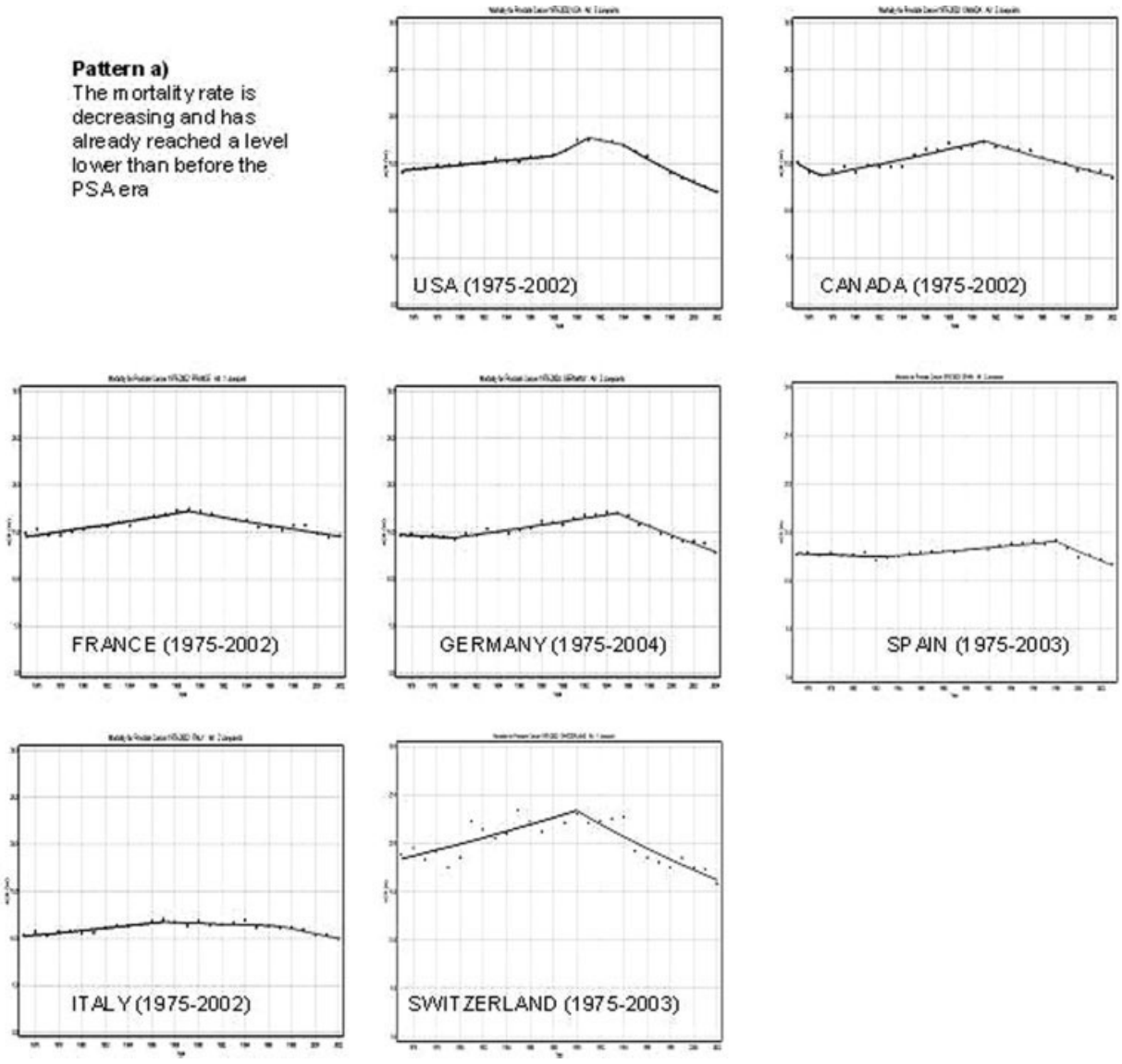

FIGURE 2 – Pattern (a). The mortality rate is decreasing and has already reached a level lower than before the PSA era. Pattern (b). The mortality rate is decreasing but still higher than the level before the PSA era. Pattern (c). The mortality rate remains increasing in a quite constant way.

Pattern c: Mortality increased

For the majority of countries, including Belgium, Denmark, Greece, Ireland, Bulgaria, Czech Republic, Belarus, Ukraine, Russian Federation, Romania, Poland, Argentina, Chile, Cuba, Mexico, Japan, Hong Kong and the Republic of Korea, prostate cancer mortality rates were still increasing (Fig. 2, pattern c). These countries showed no tendency to reduce the slope of the curve.

The momentary "hump"

In some countries with patterns (a) or (b), there was an evident "hump" (temporary increase) in prostate cancer mortality, lasting a few years and apparently coinciding with the peak of diffusion of PSA screening. This phenomenon was particularly marked in the USA data, but was present also for Hungary and Israel.

Age- and cohort analysis

Figure 3 shows that for the USA, Germany and Switzerland the recent fall in mortality was present in all age groups. Analysing the rates by birth cohorts for the same countries (Fig. 4), the risk of dying was constantly growing at elder ages in subsequent generations, before falling recently. On the contrary, in younger ages the risk was stable in subsequent cohorts, before the recent fall.

Discussion

Using the most recent available mortality data, our study confirms the decreasing trend of prostate cancer mortality in 20 of the 38 countries investigated. In 7 countries, the mortality rates are now lower than before the PSA era.

The present analysis has several strengths. The analysis is based on a very large official mortality database updated to 2002–2004. Most Western countries as well as a good sample of South American and Asian regions are included. Data show a general consistence with the expected PSA generalization. Pattern (a) is shared by several of the most affluent countries where PSA screening is probably more prevalent. For most of the countries following pattern (b) we shortly expect a change into pattern (a). In contrast,

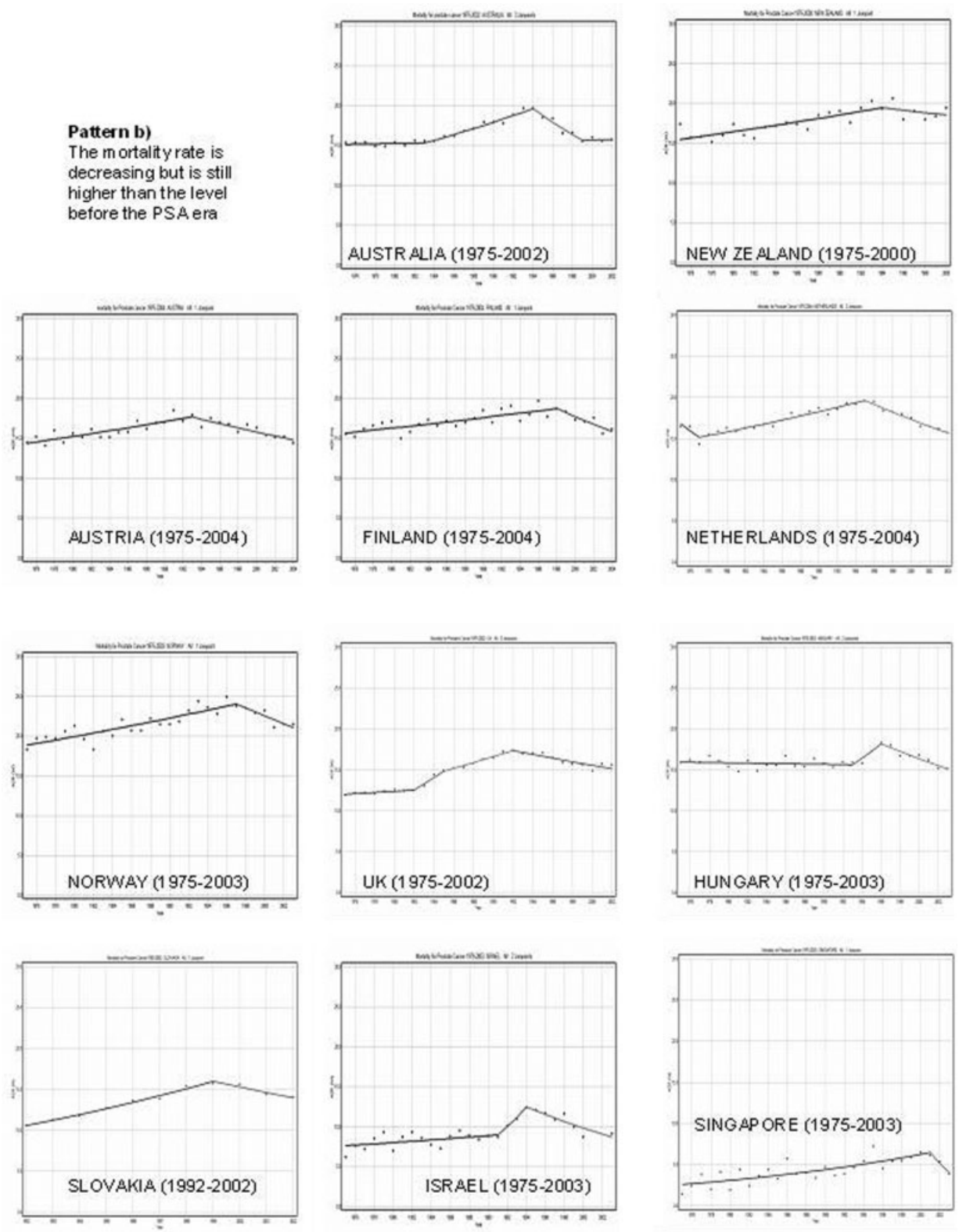

FIGURE 2 – CONTINUED

pattern (c) is more common among countries with a low or average GDP per capita, where individual cancer prevention practices are probably more limited, or in affluent countries like Denmark, where the offer of public screening programmes in general is lower than in other Nordic countries and Japan, where screenings are unusually common even as a public health policy.

However, as already largely discussed, the causal relation between PSA screening and prostate cancer mortality decrease

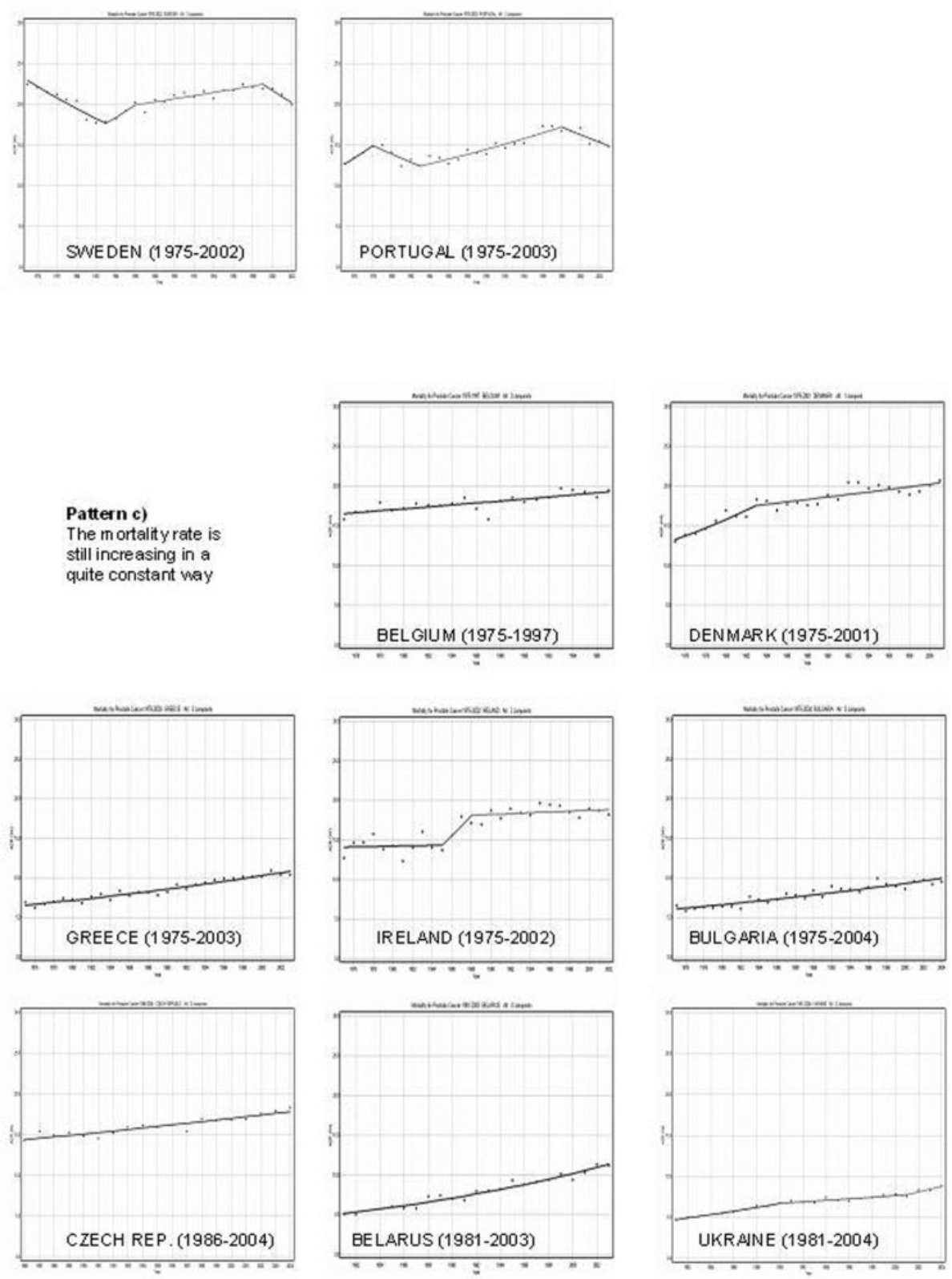

FIGURE 2 – CONTINUED

cannot be established but only supposed by a descriptive study. The observed decline in mortality can also be the consequence of treatment progress, changes in registration procedures of cause of death, or in the quality of death certification.[26] Also, we can only make hypothesis on the differences of PSA screening rates between countries because of the lack of comparable population based data on screening frequency. It would be therefore hazardous to try to statistically test the formal temporal correlation

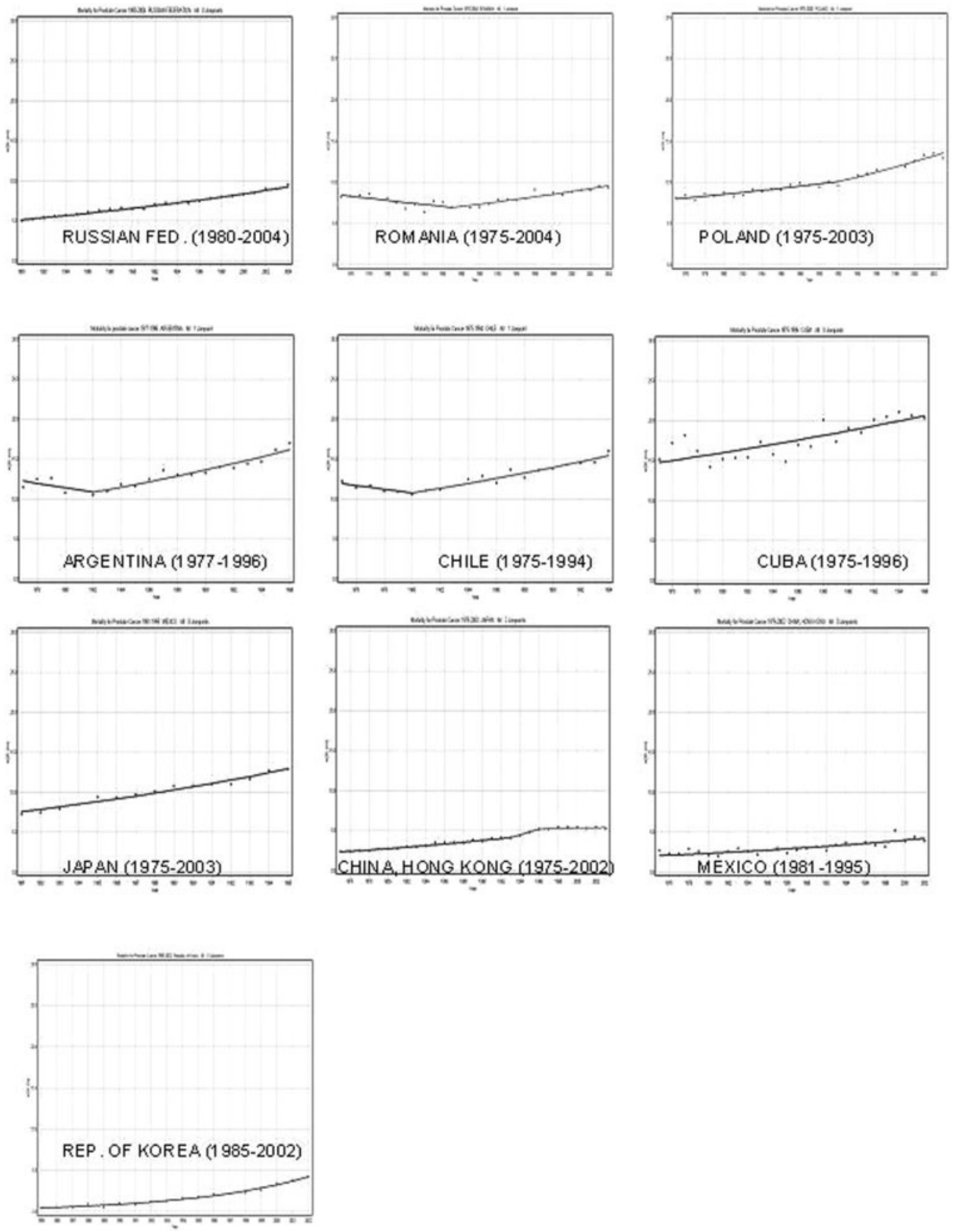

FIGURE 2 – CONTINUED

between the sparse data on intensity of PSA screening and prostate cancer mortality trends worldwide. The few available data suggest that PSA screening is more common in the USA[27] than in Europe. Within Europe, rates of screening range between 20 and 35% in countries like Austria,[20] Switzerland,[28] and France,[29,30] while North European countries such as Norway,[31] The Nertherlands,[32] and Denmark[33] present lower rates ranging from 7 to 15%.

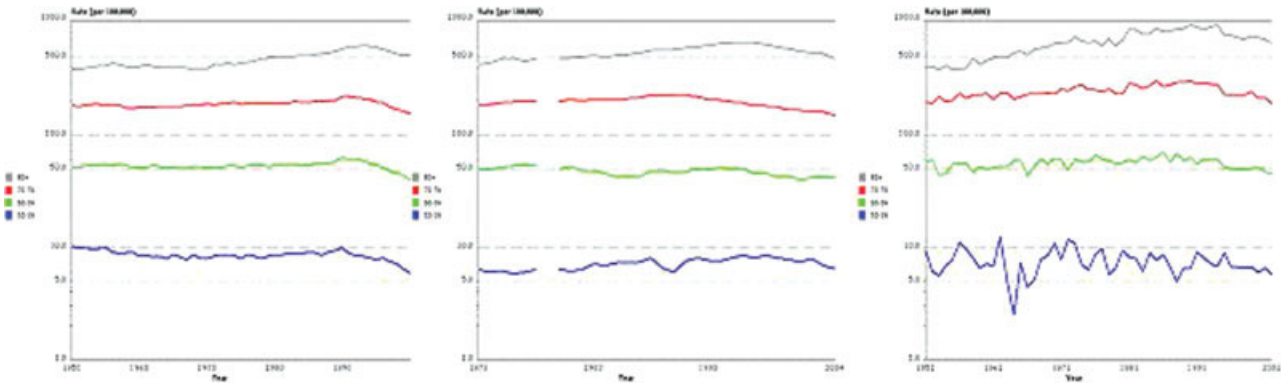

FIGURE 3 – Trend of mortality by age classes (50–59, 60–69, 70–79, 80+), respectively in USA, Germany and Switzerland.

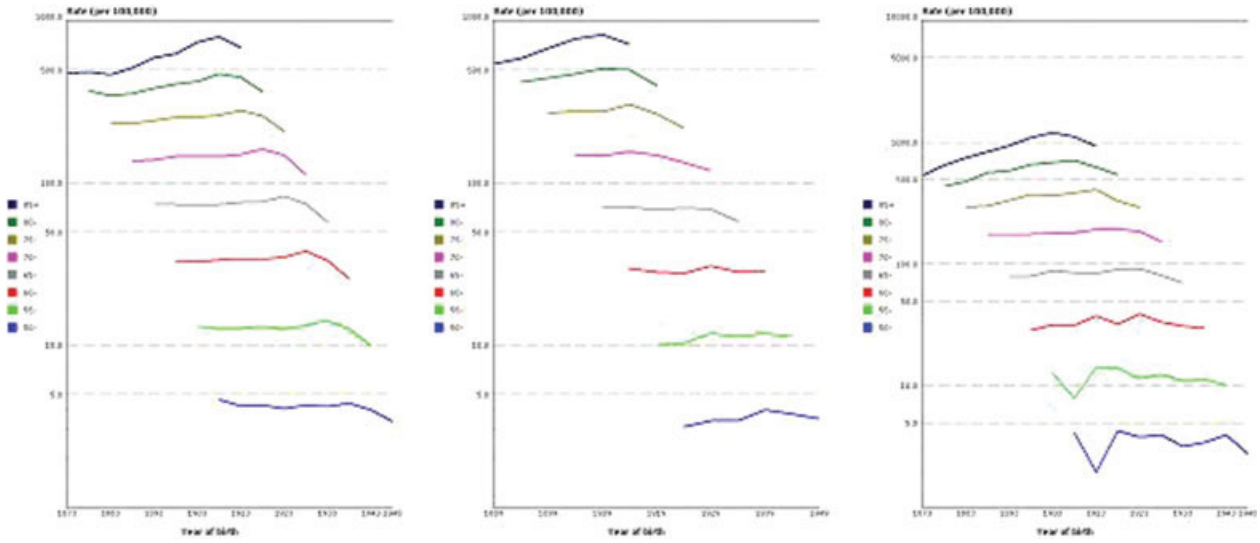

FIGURE 4 – Trend of mortality by birth cohort (50–54, 55–59, 60–64, 65–69, 70–74, 75–79, 80–84, 85+), respectively in USA, Germany and Switzerland.

The difference between the pattern (a) and (b) in mortality could also be the consequence of different patterns in the trend of the risk: a stronger decrease in mortality in countries of group (a) could be the consequence of a previous decreasing of incidence, that could not (or not yet) have been the case for countries in group (b). Such an hypothesis in not easy to test using incidence data. It would be necessary to separate the time trend of incident cases clinically diagnosed ("true incidence," "true risk") from the time trend of PSA diagnosed cases ("anticipated" incidence). After the diffusion of PSA, incidence data currently published are a mix of the two, and very few Cancer Registry worldwide are able to calculate separate incidence rates of prostate cancer anticipated by a PSA test and rates of those diagnosed after clinical onset.[34] So the time trend of the true risk, that was known before the PSA era, is now hidden in the incidence data and will remain unknown until the whole male population will be (would be) screened (end of the prevalence round of the PSA screening).

For the moment, the decrease of prostate mortality rates to levels lower than before the PSA era in USA, Canada, France, Germany, Spain, Italy and Switzerland is the only available evidence that long term prostate cancer mortality could be importantly reduced by PSA screening. This is somewhat similar to the observations made for cervical cancer screening where the first evidence of effectiveness was based on the huge decrease observed in incidence of invasive cases, but also observed in mortality data alone, for the areas not covered by cancer registration.[35]

In 3 of the countries with pattern (a) for which the decrease was more pronounced (USA, Germany and Switzerland), the analysis by age and cohort of birth shows that the recent fall in mortality regards all age groups, but that in the past the risk of dying was growing along the calendar at elder but not at younger ages. This observation shows that before the PSA era the period effect was absent and the cohort effect was present but small. A clear period effect appears after the PSA introduction:

The data also show a temporary "hump" in mortality in the mid-1990s, particularly evident in the USA. The "hump" could have been the effect of some bias on death certification more than the effect of a true increase in mortality. This point has been discussed by some authors[26,36,37] and the most credible explanation seems to be the attribution bias, *i.e.*, the attribution of the death for concurrent causes to the prostate cancer when this disease had been previously diagnosed. An alternative explanation is that a small component of the peak could also be attributed to the perioperative mortality, that has been estimated around 1% of the performed prostatectomies.[38,39]

Apart from the "hump," commenting the general trend in the USA some authors concluded that the mortality decrease was partly attributable to the PSA screening practice.[40–44] Other

authors admitted an association between the decline in mortality and the spread of PSA screening practice, but argued that the prompt fall in mortality could be explained by the hypothesis that PSA has an effect only (or mainly) on the fraction of cases with shorter pre-clinical phase.[45,46] On the other hand, Coldman *et al*. found no association between the intensity of PSA screening and the subsequent reduction in mortality.[27]

One more, concurrent or alternative, explanation for the decline in mortality could be the improvements in treatments. New surgical techniques for localized disease, new irradiation protocols and antiandrogenic therapies could have played an important role. The improvements in treatments could have become more effective in general, more effective to early stages, and more available because more emphasis is paid today on the control of prostate cancer.

In conclusion, this descriptive study confirms that mortality from prostate cancer previously observed in North America also occurs in several European countries where currently mortality rates are lower than in the pre PSA era. Waiting for the results of ongoing clinical trials, such mortality patterns strongly suggest that PSA screening could reduce prostate cancer mortality in the male population.

Mortality data deserve to be constantly monitored during the next years as an impact indicator, the more than, for prostate cancer, incidence data are no longer a good measure of the tendency of the risk (being inflated by the intensity of PSA practice) and survival data are biased on their turn by the anticipation due to the screening.

Acknowledgements

The authors thank Ms. Stina Blagojevic and Ms. Simona Gallo for their technical help and editorial assistance, Dr. Isabelle Neyroud-Caspar, Ms. Hyma Schubert and Mr. David James and the Association Prosca (Prostate Cancer Patient Association, Geneva Switzerland) for reviewing our study and for her helpful comments on the manuscript, and the Cancer Registry team for providing data and support.

References

1. De Koning HJ, Auvinen A, Berenguer SA, Calais dS, Ciatto S, Denis L, Gohagan JK, Hakama M, Hugosson J, Kranse R, Nelen V, Prorok PC, et al. Large-scale randomized prostate cancer screening trials: program performances in the European randomized screening for prostate cancer trial and the prostate, lung, colorectal and ovary cancer trial. Int J Cancer 2002;97:237–44.
2. Gohagan JK, Prorok PC, Kramer BS, Cornett JE. Prostate cancer screening in the prostate, lung, colorectal and ovarian cancer screening trial of the national cancer institute. J Urol 1994;152:1905–9.
3. Andriole GL, Levin DL, Crawford ED, Gelmann EP, Pinsky PF, Chia D, Kramer BS, Reding D, Church TR, Grubb RL, Izmirlian G, Ragard LR, et al. Prostate cancer screening in the prostate, lung, colorectal and ovarian (PLCO) Cancer. screening trial: findings from the initial screening round of a randomized trial. J Natl Cancer Inst 2005; 97:433–8.
4. Schroder FH, Denis LJ, Roobol M, Nelen V, Auvinen A, Tammela T, Villers A, Rebillard X, Ciatto S, Zappa M, Berenguer A, Paez A, et al. The story of the European randomized study of screening for prostate cancer. BJU Int 2003;92(Suppl 2):1–13.
5. De Koning HJ, Liem MK, Baan CA, Boer R, Schroder FH, Alexander FE. Prostate cancer mortality reduction by screening: power and time frame with complete enrollment in the European randomised screening for prostate cancer (ERSPC) trial. Int J Cancer 2002;98: 268–73.
6. Swan J, Breen N, Coates RJ, Rimer BK, Lee NC. Progress in cancer screening practices in the United States: results from the 2000 national health interview survey. Cancer 2003;97:1528–40.
7. Melia J, Moss S. Survey of the rate of PSA testing in general practice. Br J Cancer 2001;85:656–7.
8. Oliver SE, May MT, Gunnell D. International trends in prostate-cancer mortality in the "PSA ERA". Int J Cancer 2001;92:893–8.
9. Curado MP, Edwards B, Shin HR, Storm H, Ferlay J, Heanue M, Boyle P, eds. Cancer incidence in five continents, vol. 9. Lyon: IARC, 2007. IARC Scientific Publications No. 160.
10. Berrino F, De Angelis R, Sant M, Rosso S, Bielska-Lasota M, Coebergh JW, Santaquilani M; EUROCARE working group. Survival for eight major cancers and all cancers combined for European adults diagnosed in 1995–99: results of the EUROCARE-4 study. Lancet Oncol 2007;8:773–83. Erratum in: Lancet Oncol 2007 Oct;8:868. Lasota, Magdalena B [corrected to Bielska-Lasota, Magdalena]. PMID: 17714991.
11. Vutuc C, Waldhoer T, Madersbacher S, Micksche M, Haidinger G. Prostate cancer in Austria: impact of prostate-specific antigen test on incidence and mortality. Eur J Cancer Prev 2001;10:425–8.
12. Sarma AV, Schottenfeld D. Prostate cancer incidence, mortality, and survival trends in the United States: 1981–2001. Semin Urol Oncol 2002;20:3–9.
13. Quinn M, Babb P. Patterns and trends in prostate cancer incidence, survival, prevalence and mortality. Part I: international comparisons. BJU Int 2002;90:162–73.
14. Stephenson RA. Prostate cancer trends in the era of prostate-specific antigen. An update of incidence, mortality, and clinical factors from the SEER database. Urol Clin North Am 2002;29:173–81.
15. Chu KC, Tarone RE, Freeman HP. Trends in prostate cancer mortality among black men and white men in the United States. Cancer 2003;97:1507–16.
16. Evans HS, Moller H. Recent trends in prostate cancer incidence and mortality in Southeast England. Eur Urol 2003;43:337–41.
17. McDavid K, Lee J, Fulton JP, Tonita J, Thompson TD. Prostate cancer incidence and mortality rates and trends in the United States and Canada. Public Health Rep 2004;119:174–86.
18. Levi F, Lucchini F, Negri E, Boyle P, La Vecchia C. Leveling of prostate cancer mortality in Western Europe. Prostate 2004;60:46–52.
19. Horninger W, Berger A, Pelzer A, Klocker H, Oberaigner W, Schonitzer D, Severi G, Robertson C, Boyle P, Bartsch G. Screening for prostate cancer: updated experience from the Tyrol study. Can J Urol 2005;12(Suppl 1):7–13.
20. Oberaigner W, Horninger W, Klocker H, Schonitzer D, Stuhlinger W, Bartsch G. Reduction of prostate cancer mortality in Tyrol. Austria, after introduction of prostate-specific antigen testing. Am J Epidemiol 2006;164:376–84.
21. Quaglia A, Parodi S, Grosclaude P, Martinez-Garcia C, Coebergh JW, Vercelli M. Differences in the epidemic rise and decrease of prostate cancer among geographical areas in Southern Europe. An analysis of differential trends in incidence and mortality in France, Italy and Spain. Eur J Cancer 2003;39:654–65.
22. Stracci F, Canosa A, Minelli L, Petrinelli AM, Cassetti T, Romagnoli C, La Rosa F. Cancer mortality trends in the Umbria region of Italy 1978–2004: a joinpoint regression analysis. BMC Cancer 2007;7:10.
23. Baade PD, Coory MD, Aitken JF. International trends in prostate-cancer mortality: the decrease is continuing and spreading. Cancer Causes Control 2004;15:237–41.
24. International Agency for Research on Cancer (IARC). CancerMondial. http://www-dep.iarc.fr/. Access date February 2007.
25. National Cancer Institute, National cancer insti. Statistical research and applications. Joinpoint Regression Program. http://srab.cancer.gov/joinpoint/.
26. Feuer EJ, Merrill RM, Hankey BF. Cancer surveillance series: interpreting trends in prostate cancer–part II: cause of death misclassification and the recent rise and fall in prostate cancer mortality. J Natl Cancer Inst 1999;91:1025–32.
27. Coldman AJ, Phillips N, Pickles TA. Trends in prostate cancer incidence and mortality: an analysis of mortality change by screening intensity. CMAJ 2003;168:31–5.
28. Bouchardy C, Boggio P, Rapin CH, Deom A, Iselin C. [Prostate cancer screening in Geneva: a physician survey]. Le dépistage du cancer de la prostate à Genève: une étude auprès des médecins traitants. Bull. Suisse. Cancer 2004;2400:91–4.
29. Vincendeau S, Abi MM, Manunta A, Patard JJ, Guille F, Lobel B. [PSA: the difficult position of general practitioners between patients and urologists]. Prog Urol 2003;13:252–5.
30. Menegoz F, Colonna M, Exbrayat C, Mousseau M, Orfeuvre H, Schaerer R. A recent increase in the incidence of prostatic carcinoma in a French population: role of ultrasonography and prostatic specific antigen. Eur J Cancer 1995;31A:55–8.
31. Skovlund E, Fossa SD. [PSA analyses in three Norwegian counties in 1999]. Tidsskr Nor Laegeforen 2000;120:2539–41.
32. Beemsterboer PM, De Koning HJ, Kranse R, Trienekens PH, Van der Maas PJ, Schroder FH. Prostate specific antigen testing and digital rectal examination before and during a randomized trial of screening for prostate cancer: European randomized study of screening for prostate cancer. Rotterdam. J Urol 2000;164:1216–20.
33. Jonler M, Eddy B, Poulsen J. Prostate-specific antigen testing in general practice: a survey among 325 general practitioners in Denmark. Scand J Urol Nephrol 2005;39:214–8.

34. Etzioni R, Penson DF, Legler JM, di Tommaso D, Boer R, Gann PH, Feuer EJ. Overdiagnosis due to prostate-specific antigen screening: lessons from U.S. prostate cancer incidence trends. J Natl Cancer Inst 2002;94:981–90.
35. IARC Handbook of cancer prevention n. 10, Cervix Cancer Screening. IARC, Lyon 2005.
36. Hoffman RM, Stone SN, Hunt WC, Key CR, Gilliland FD. Effects of misattribution in assigning cause of death on prostate cancer mortality rates. Ann Epidemiol 2003;13:450–4.
37. Lu-Yao G, Stukel TA, Yao SL. Changing patterns in competing causes of death in men with prostate cancer: a population based study. J Urol 2004;171:2285–90.
38. Viville C. Total prostatectomy for cancer. Mortality and morbidity. Apropos of 1288 operations. The ANFUC survey. J Urol (Paris) 1994; 100:3–7.
39. Huland H. The risk outweigh the benefits of radical prostatectomy in localised prostate cancer: the argument against. Eur Urol 1996; 29(Suppl 2):31–3.
40. Gilliland F, Becker TM, Smith A, Key CR, Samet JM. Trends in prostate cancer incidence and mortality in New Mexico are consistent with an increase in effective screening. Cancer Epidemiol Biomarkers Prev 1994;3:105–11.
41. Mettlin C. Impact of screening on prostate cancer rates and trends. Microsc Res Tech 2000;51:415–8.
42. Hankey BF, Feuer EJ, Clegg LX, Hayes RB, Legler JM, Prorok PC, Ries LA, Merrill RM, Kaplan RS. Cancer surveillance series: interpreting trends in prostate cancer–part I: evidence of the effects of screening in recent prostate cancer incidence, mortality, and survival rates. J Natl Cancer Inst 1999;91:1017–24.
43. Feuer EJ, Mariotto A, Merrill R. Modeling the impact of the decline in distant stage disease on prostate carcinoma mortality rates. Cancer 2002;95:870–80.
44. Roberts RO, Bergstralh EJ, Katusic SK, Lieber MM, Jacobsen SJ. Decline in prostate cancer mortality from 1980 to 1997, and an update on incidence trends in Olmsted county, Minnesota. J Urol 1999;161: 529–33.
45. Vis AN. Does PSA screening reduce prostate cancer mortality? CMAJ 2002;166:600–1.
46. Etzioni R, Legler JM, Feuer EJ, Merrill RM, Cronin KA, Hankey BF. Cancer surveillance series: interpreting trends in prostate cancer. III. quantifying the link between population prostate-specific antigen testing and recent declines in prostate cancer mortality. J Natl Cancer Inst 1999;91:1033–9.