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## Platinum Priority – Bladder Cancer

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# Economic Burden of Bladder Cancer Across the European Union

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### Abstract

**Background:** More than 120 000 people are diagnosed annually with bladder cancer in the 28 countries of the European Union (EU). With >40 000 people dying of it each year, it is the sixth leading cause of cancer. However, to date, no systematic cost-of-illness study has assessed the economic impact of bladder cancer in the EU.

**Objective:** To estimate the annual economic costs of bladder cancer in the EU for 2012. **Design, setting, and participants:** Country-specific cancer cost data were estimated using aggregate data on morbidity, mortality, and health care resource use, obtained from numerous international and national sources.

**Outcome measurements and statistical analysis:** Health care costs were estimated from expenditures on primary, outpatient, emergency, and inpatient care, as well as medications. Costs of unpaid care and lost earnings due to morbidity and early death were estimated.

**Results and limitations:** Bladder cancer cost the EU €4.9 billion in 2012, with health care accounting for €2.9 billion (59%) and representing 5% of total health care cancer costs. Bladder cancer accounted for 3% of all cancer costs in the EU (€143 billion) in 2012 and represented an annual health care cost of €57 per 10 EU citizens, with costs varying >10 times between the country with the lowest cost, Bulgaria (€8 for every 10 citizens), and highest cost, Luxembourg (€93). Productivity losses and informal care represented 23% and 18% of bladder cancer costs, respectively. The quality and availability of comparable cancer-related data across the EU need further improvement.

**Conclusions:** Our results add to essential public health and policy intelligence for delivering affordable bladder cancer care systems and prioritising the allocation of public research funds.

**Patient summary:** We looked at the economic costs of bladder cancer across the European Union (EU). We found bladder cancer to cost €4.9 billion in 2012, with health care accounting for €2.9 billion. Our study provides data that can be used to inform affordable cancer care in the EU.

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## 1. Introduction

Cancer is a major health problem in the European Union (EU). In 2009 it cost the health care systems of the 27 countries in the EU €51 billion, representing 4% of total

health care expenditures [1]. Including the burden associated with lost earnings, both from early mortality and absence from work, and the costs of informal care, whereby relatives and/or friends provided unpaid care for people with cancer, the costs increased to €126 billion.

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Although the study by Luengo-Fernandez et al (2013) [1] quantified the costs for breast, colorectal, lung, and prostate cancer, it did not evaluate how much of total cancer costs could be attributed to bladder cancer. Bladder cancer is the sixth leading cause of cancer in the EU [2], with 124 000 people diagnosed and >40 000 people dying from the disease each year. By 2030 the annual incidence is projected to increase to 219 000, two-fifths of this due to the ageing of the European population [2]. Planning urologic care systems across Europe requires not only good epidemiology but also investment and cost-effective treatments and pathways. Critical to these calculations is the macroeconomic impact of bladder cancer.

The aim of this study is to evaluate the economic burden of bladder cancer across the 28 countries that made up the EU in 2012. We included health care and non-health care costs and also updated the economic burden of all cancers for 2012.

## 2. Methods

Cancer was defined by the World Health Organisation International Classification of Diseases, 10th revision, as codes C00–C97, and bladder cancer was defined as C67. For all countries we used the same methodological framework to obtain data and value cancer-related resource use [1,3,4]. An annual time frame was adopted, whereby resource use attributable to cancer and bladder cancer within the most recent year for which data were available were measured, regardless of disease onset. Resource use was valued by applying country-specific unit costs. Costs were converted to 2012 prices [5], and national currencies were converted to euros (€) using 2012 exchange rates. To allow comparisons between countries, we also adjusted for cost of living using the purchasing power parity (PPP) method [6]. This method measures the price of the same bundle of goods in different countries and allows comparisons of costs adjusted for differences in the cost of living between countries.

International and national sources were consulted for country-specific aggregate data (see Supplement 1 for more detail). We also consulted peer-reviewed published studies or national reports from governmental or professional bodies. If no data were found, extrapolations were performed from similar countries (eg, similar health care expenditure per person, life expectancy, and geographic location).

### 2.1. Health care expenditure

Cancer health care service included primary care, accident and emergency (A&E) care, hospital inpatient care, outpatient care, and medications (see Supplement 1 for methodology, data sources, and the quality of each data estimate). Other types of activities relating to the prevention of cancer such as health education in community-based settings were not included because of the difficulties in identifying activity levels.

Country-specific pharmaceutical expenditures on cancer for 2009 were obtained. This consisted of sales of antineoplastic agents and endocrine treatment (Anatomical Therapeutic Chemical codes L1 and L2) [1]. Expenditures for 2009 were updated to 2012 by assuming a 4.6% annual growth in cancer-related pharmaceutical expenditures [7]. Due to the absence of EU-level data on cancer-related pharmaceutical expenditures due to bladder cancer, this proportion (4%) was obtained from reports from Germany (2%) and the Netherlands (6%) and applied to the remaining countries [8,9].

### 2.2. Informal care costs

Informal care costs were equivalent to the opportunity cost of unpaid care, that is, the time (work and/or leisure) that caregivers forgo, valued

in monetary terms, to provide unpaid care for relatives with cancer. We used country-specific data from the International Agency for Research on Cancer (IARC) [2] to estimate the number of people with cancer and bladder cancer and data from the Survey of Health, Ageing and Retirement in Europe [10] to assess the hours of informal care needed by cancer and bladder cancer patients (see Supplement 1).

### 2.3. Productivity losses

Productivity costs included the foregone earnings related to cancer-attributable mortality and morbidity. For all countries we assumed an initial working age of 15 yr. Age- and gender-specific deaths due to cancer and bladder cancer were obtained for all countries from Eurostat [11]. The potential working-years lost was estimated as the difference between the age at death and maximum age of retirement (which we set at 79 yr). However, this would overestimate the total working-years lost because not everyone will be economically active (ie, either working or actively searching for work) or employed. Therefore, age- and gender-specific unemployment and activity rates for each of the 28 countries were applied to the potential foregone earnings due to premature mortality [12]. The total number of working-years lost was then multiplied by gender-specific average annual earnings [13]. Future earnings lost due to mortality were discounted to present values using a 3.5% annual rate (ie, the value society attaches to present as opposed to future costs).

Costs due to cancer-related morbidity comprised both the costs associated with individuals declared incapacitated or disabled because of cancer (permanent absence) and the costs due to individuals taking sickness leave for a defined time period (temporary absence) (see Supplement 1). Costs were estimated by multiplying the total working time lost due to cancer by mean earnings [12]. We used the friction period approach because absent workers are likely to be replaced, whereby costs for temporary and permanent absences were counted only during the time taken to replace a worker (first 90 d of work absence).

### 2.4. Noneconomic burden

We obtained noneconomic measures of burden of cancer and bladder cancer including number of deaths [11], incident disease cases [2], prevalent disease cases (5 yr) [2], and disability-adjusted life years (DALYs) lost. The rate, per 100 000 in the population, of DALYs lost for cancer and bladder cancer was obtained for 2010 [14] and applied to 2012 population estimates [15].

### 2.5. Statistical analysis

We explored variations between countries in cancer-related health care costs per capita using ordinary least squares (OLS) univariate regression analyses conditional on national income (per capita), health care expenditure (per capita), cancer incidence (crude rate), cancer mortality (crude rate), mortality-to-incidence ratio (MIR), proportion of the population who smoke, and cancer-specific DALYs (rate per 100 000). An explanatory variable was significant if its *p* value was <0.05. All regression analyses were performed using Stata software v.12.1 (StataCorp, College Station, TX, USA).

### 2.6. Sensitivity analysis

We estimated the effects on the total costs of bladder cancer of changes in (1) health care resource use (all categories) and earnings (male and female) across all countries, (2) proportion of cancer-related pharmaceutical expenditure due to bladder cancer (2% and 6%), (3) discounting rate for productivity losses due to early mortality, and (4) no friction period for costs due to cancer-related morbidity.

**Table 1 – Noneconomic burden of cancers and bladder cancer**

| Country        | Deaths    |                | Incidence |                | Prevalence, 5-yr data |                | DALYs      |                |
|----------------|-----------|----------------|-----------|----------------|-----------------------|----------------|------------|----------------|
|                | Cancer    | Bladder cancer | Cancer    | Bladder cancer | Cancer                | Bladder cancer | Cancer     | Bladder cancer |
| Austria        | 19 757    | 490            | 40 973    | 2159           | 114 793               | 7492           | 363 264    | 7811           |
| Belgium        | 27 367    | 926            | 65 056    | 4348           | 192 018               | 14 220         | 554 321    | 12 670         |
| Bulgaria       | 16 562    | 485            | 31 884    | 1662           | 75 554                | 4958           | 375 315    | 9496           |
| Croatia        | 13 481    | 366            | 22 776    | 1053           | 61 969                | 3709           | 243 436    | 5362           |
| Cyprus         | 1110      | 45             | 3417      | 227            | 10 420                | 803            | 27 652     | 734            |
| Czech Republic | 27 834    | 767            | 57 461    | 2462           | 145 631               | 8192           | 584 071    | 14 014         |
| Denmark        | 14 886    | 492            | 35 984    | 1781           | 92 520                | 5607           | 300 846    | 9146           |
| Estonia        | 3550      | 106            | 6095      | 209            | 14 791                | 607            | 59 171     | 1374           |
| Finland        | 11 579    | 252            | 28 300    | 1093           | 83 641                | 3781           | 214 365    | 4040           |
| France         | 155 331   | 5112           | 370 228   | 11 166         | 1 121 491             | 34 160         | 3 280 323  | 85 854         |
| Germany        | 218 889   | 5516           | 491 825   | 28 403         | 1 396 766             | 100 676        | 4 237 296  | 105 824        |
| Greece         | 27 159    | 1031           | 40 794    | 2777           | 101 880               | 9673           | 506 209    | 18 542         |
| Hungary        | 32 460    | 904            | 50 286    | 2689           | 113 182               | 8057           | 656 401    | 14 103         |
| Ireland        | 8094      | 188            | 20 655    | 666            | 54 920                | 2106           | 161 838    | 2979           |
| Italy          | 167 251   | 5701           | 353 184   | 18 281         | 1 012 541             | 65 153         | 2 985 331  | 94 377         |
| Latvia         | 6039      | 200            | 10 304    | 425            | 24 462                | 1233           | 101 110    | 2574           |
| Lithuania      | 8110      | 248            | 14 462    | 569            | 34 785                | 1647           | 143 397    | 3163           |
| Luxembourg     | 1018      | 42             | 2475      | 96             | 8264                  | 540            | 22 329     | 469            |
| Malta          | 840       | 33             | 1893      | 131            | 5207                  | 492            | 16 748     | 463            |
| Netherlands    | 42 359    | 1228           | 93 015    | 2999           | 267 924               | 10 296         | 835 530    | 21 415         |
| Poland         | 92 610    | 3111           | 151 517   | 7960           | 350 227               | 23 566         | 1 969 546  | 55 534         |
| Portugal       | 24 978    | 810            | 48 855    | 2874           | 134 272               | 8804           | 510 242    | 12 841         |
| Romania        | 47 307    | 1391           | 78 316    | 3824           | 178 416               | 11 272         | 972 887    | 23 110         |
| Slovakia       | 12 073    | 303            | 23 919    | 933            | 56 296                | 2666           | 269 049    | 4886           |
| Slovenia       | 5834      | 184            | 11 407    | 463            | 28 909                | 1292           | 104 851    | 2460           |
| Spain          | 103 307   | 4936           | 214 588   | 13 789         | 581 688               | 47 225         | 2 028 353  | 73 973         |
| Sweden         | 21 646    | 684            | 50 262    | 2350           | 156 481               | 7885           | 387 014    | 9919           |
| United Kingdom | 157 581   | 4914           | 326 273   | 8776           | 827 126               | 27 410         | 2 913 926  | 69 591         |
| TOTAL EU       | 1 269 012 | 40 465         | 2 646 204 | 124 165        | 7 246 174             | 413 522        | 24 824 821 | 666 726        |

DALY = disability-adjusted life year; EU = European Union.

### 3. Results

#### 3.1. Noneconomic burden

In 2012 cancer was diagnosed in 2.6 million people; 124 000 of these were due to bladder cancer (5%; Table 1). More than 7 million people were estimated to be either living with or having survived cancer, with 410 000 (6%) due to bladder cancer. Approximately 1.3 million people died of cancer; 3% of these were due to bladder cancer (Table 1). Furthermore, 25 million DALYs were due to cancer, of which >660 000 were due to bladder cancer (3%).

#### 3.2. Economic burden of bladder cancer

Bladder cancer cost the EU €4.9 billion in 2012 (Table 2 and Supplementary Table 5). The five most populous countries (ie, France, Germany, Italy, Spain, and the United Kingdom) accounted for €3.6 billion (73% of all costs).

Bladder cancer cost EU health care systems €2.9 billion in 2012 (Table 2), representing 59% of the total economic burden. Inpatient care was the major cost component, accounting for 58% (€1.7 billion) of health care costs, followed by expenditures on drugs at €568 million (20% of total health care costs). Annual health care costs of bladder cancer were equivalent to €57 per every 10 EU citizens

(Fig. 1) but varied widely between countries, with a 12-time difference between the lowest (Bulgaria: €8 for every 10 citizens) and highest cost per capita (Luxembourg: €93 for every 10 citizens). Health care costs were €6942 per prevalent case, but these also varied considerably between countries, with a five-time difference between the lowest (Latvia: €2257) and highest spender (France: €11 937), after adjusting for price differentials (Supplementary Fig. 1).

The OLS regression showed a strong positive association between bladder cancer health care costs (per capita and per prevalent case) and national health care expenditures ( $p < 0.01$ ) and national income ( $p < 0.01$ ). No significant associations between bladder cancer health care costs (per capita and per prevalence case) and incidence, mortality, MIR, smoking rates, and DALYs were identified (Supplementary Figures 3–9).

Unpaid care accounted for >88 million hours with a cost of €900 million (18% of total costs; Table 2). Approximately 34 000 working-years were lost due to mortality, which were valued at €770 million (16% of total costs). We estimated that 3 million working-days were lost in 2012 due to cancer-related morbidity, which, when adjusted using the friction period, accounted for €330 million (7% of the total economic burden).

Sensitivity analysis showed that a 20% variation in health care resource use had the biggest impact on total bladder cancer costs (12% change), with the resulting total costs

**Table 2 – Costs of bladder cancer (€ thousands) in the European Union, by country, 2012**

| Country        | Health care costs |                 |        |                |             |                   | Total cancer health expenditure, % | Productivity losses |           | Informal care costs | Total costs |                      |
|----------------|-------------------|-----------------|--------|----------------|-------------|-------------------|------------------------------------|---------------------|-----------|---------------------|-------------|----------------------|
|                | Primary care      | Outpatient care | A&E    | Inpatient care | Medications | Total health care |                                    | Mortality           | Morbidity |                     | Total       | Total cancer cost, % |
| Austria        | 1617              | 2709            | 1105   | 34 680         | 15 784      | 55 895            | 4                                  | 13 126              | 9 976     | 12 153              | 91 151      | 3                    |
| Belgium        | 2453              | 4879            | 651    | 33 763         | 15 922      | 57 668            | 5                                  | 17 998              | 18 820    | 26 503              | 120 990     | 3                    |
| Bulgaria       | 416               | 493             | 70     | 2555           | 2003        | 5538              | 4                                  | 2776                | 1905      | 1567                | 11 785      | 3                    |
| Croatia        | 1053              | 588             | 2039   | 2110           | 3382        | 9172              | 4                                  | 4537                | 5382      | 2881                | 21 972      | 3                    |
| Cyprus         | 119               | 312             | 123    | 393            | 995         | 1941              | 6                                  | 1130                | 316       | 1196                | 4584        | 4                    |
| Czech Republic | 2793              | 6836            | 1320   | 14 964         | 9213        | 35 126            | 6                                  | 7572                | 7503      | 6392                | 56 594      | 4                    |
| Denmark        | 301               | 898             | 264    | 11 789         | 9416        | 22 668            | 4                                  | 21 009              | 15 804    | 25 656              | 85 137      | 3                    |
| Estonia        | 272               | 496             | 237    | 1485           | 478         | 2967              | 4                                  | 1083                | 598       | 675                 | 5323        | 3                    |
| Finland        | 1440              | 9020            | 1302   | 17 395         | 7202        | 36 360            | 4                                  | 6817                | 1 663     | 7557                | 52 397      | 3                    |
| France         | 10 062            | 15 951          | 1938   | 289 682        | 139 084     | 456 717           | 5                                  | 97 052              | 47 475    | 101 911             | 703 154     | 3                    |
| Germany        | 45 531            | 37 469          | 989    | 461 769        | 64 208      | 609 965           | 4                                  | 157 594             | 78 163    | 170 065             | 1 015 787   | 3                    |
| Greece         | 4317              | 9649            | 1909   | 34 199         | 13 250      | 63 323            | 6                                  | 10 594              | 4651      | 14 035              | 92 603      | 4                    |
| Hungary        | 1311              | 2031            | 338    | 7305           | 10 169      | 21 155            | 3                                  | 6561                | 1606      | 5671                | 34 994      | 3                    |
| Ireland        | 1350              | 1410            | 745    | 10 450         | 5828        | 19 782            | 3                                  | 6829                | 1474      | 4542                | 32 627      | 2                    |
| Italy          | 60 396            | 67 557          | 45 120 | 284 646        | 76 499      | 534 216           | 7                                  | 80 530              | 7671      | 192 078             | 814 495     | 5                    |
| Latvia         | 312               | 722             | 63     | 1029           | 511         | 2638              | 4                                  | 1382                | 494       | 1155                | 5669        | 3                    |
| Lithuania      | 480               | 470             | 138    | 1184           | 399         | 2671              | 4                                  | 1875                | 685       | 1065                | 6296        | 3                    |
| Luxembourg     | 285               | 516             | 39     | 2877           | 1183        | 4900              | 5                                  | 1612                | 884       | 1425                | 8821        | 4                    |
| Malta          | 27                | 44              | 16     | 411            | 555         | 1053              | 5                                  | 405                 | 45        | 511                 | 2012        | 4                    |
| Netherlands    | 9043              | 13 858          | 1206   | 93 303         | 16 422      | 133 832           | 5                                  | 50 550              | 16 564    | 28 717              | 229 663     | 3                    |
| Poland         | 9042              | 28 015          | 1034   | 30 337         | 11 977      | 80 405            | 6                                  | 33 293              | 20 825    | 22 216              | 156 740     | 4                    |
| Portugal       | 4567              | 7541            | 1877   | 7323           | 11 342      | 32 649            | 5                                  | 19 678              | 4738      | 13 915              | 70 980      | 3                    |
| Romania        | 854               | 2834            | 127    | 6188           | 8939        | 18 942            | 4                                  | 11 885              | 4849      | 5560                | 41 237      | 3                    |
| Slovakia       | 2005              | 4874            | 245    | 3805           | 5129        | 16 058            | 5                                  | 1909                | 2663      | 2050                | 22 680      | 3                    |
| Slovenia       | 217               | 459             | 297    | 4159           | 2151        | 7283              | 4                                  | 2709                | 3508      | 2514                | 16 014      | 3                    |
| Spain          | 43 539            | 25 406          | 14 636 | 131 669        | 69 662      | 284 912           | 5                                  | 65 856              | 19 621    | 128 151             | 498 540     | 4                    |
| Sweden         | 4665              | 15 309          | 3618   | 30 240         | 12 585      | 66 416            | 5                                  | 17 313              | 21 533    | 18 404              | 123 666     | 4                    |
| United Kingdom | 3793              | 71 664          | 4192   | 153 029        | 53 702      | 286 380           | 5                                  | 126 204             | 29 754    | 101 291             | 543 630     | 3                    |
| TOTAL EU       | 212 258           | 332 009         | 85 637 | 1 672 739      | 567 991     | 2 870 634         | 5                                  | 769 879             | 329 170   | 899 857             | 4 869 542   | 3                    |

A&amp;E = accident and emergency; EU = European Union.

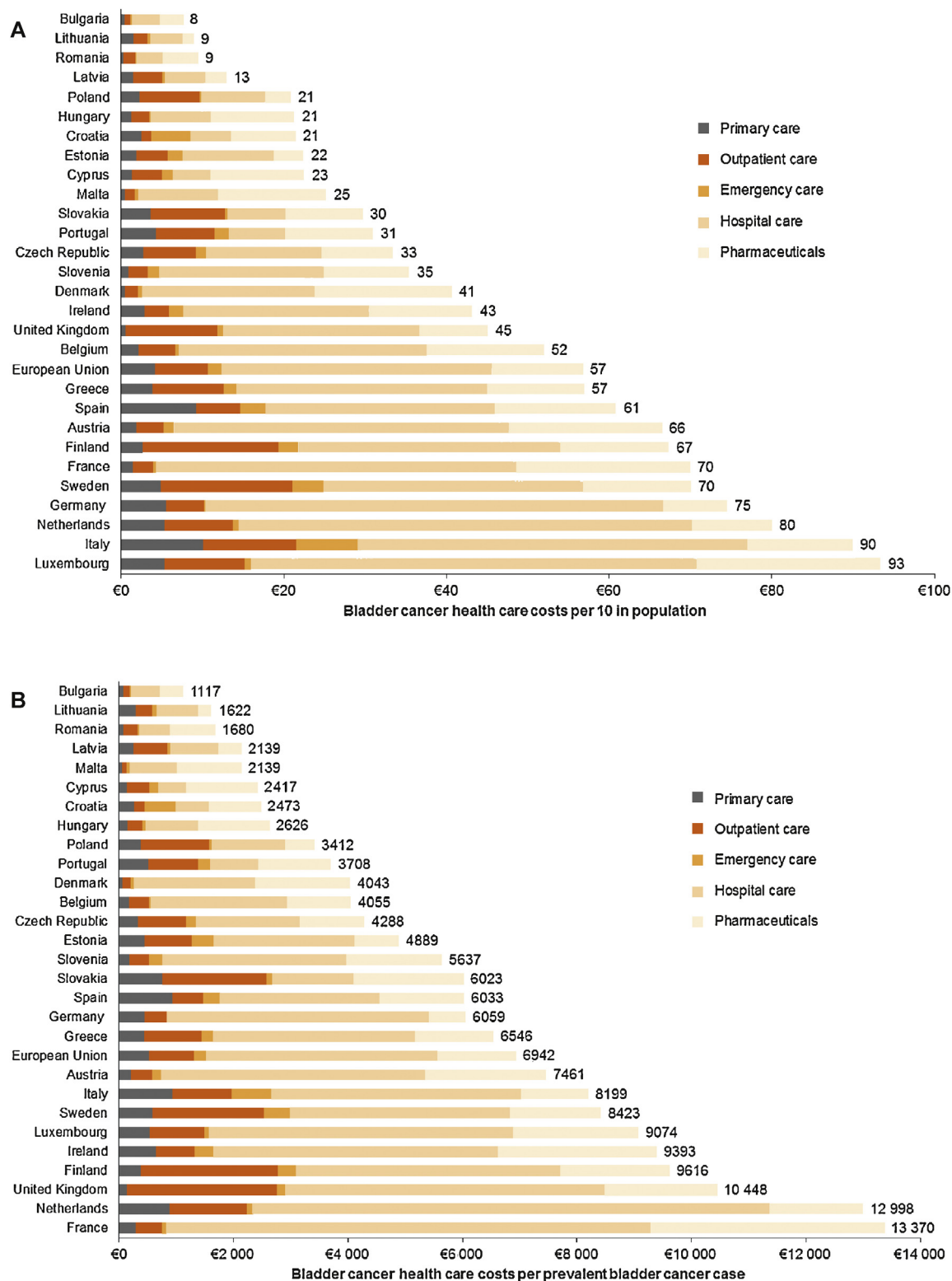


Fig. 1 – Total health care costs (€), not adjusted for price differentials, of bladder cancer by health care service category (A) per 10 in the population, 2012, and (B) per prevalent bladder cancer case.

varying between €4.3 and €5.4 billion (Supplementary Fig. 10). The 20% variation in earnings resulted in an 8% change on total bladder cancer costs, with these varying between €4.5 and €5.3 billion.

### 3.3. Bladder cancer as a proportion of total cancer costs

The total cancer costs in the EU were estimated at €143 billion in 2012 (Table 3 and Supplementary Table 8),

**Table 3 – Costs of cancer (€ thousands) in the European Union, by country, 2012**

| Country        | Health care costs |                 |           |                |             |                   | Total health expenditure, % | Productivity losses |            | Informal care costs | Total costs |        |
|----------------|-------------------|-----------------|-----------|----------------|-------------|-------------------|-----------------------------|---------------------|------------|---------------------|-------------|--------|
|                | Primary care      | Outpatient care | A&E       | Inpatient care | Medications | Total health care |                             | Mortality           | Morbidity  |                     | Total       | GDP, % |
| Austria        | 35 888            | 60 134          | 24 517    | 842 330        | 392 932     | 1 355 801         | 4                           | 1 062 446           | 369 546    | 357 421             | 3 145 215   | 1.02   |
| Belgium        | 35 515            | 70 632          | 9418      | 702 639        | 396 369     | 1 214 574         | 3                           | 1 263 559           | 783 295    | 627 126             | 3 888 554   | 1.03   |
| Bulgaria       | 9240              | 10 964          | 1565      | 56 170         | 49 861      | 127 799           | 5                           | 159 855             | 41 868     | 42 949              | 372 472     | 0.93   |
| Croatia        | 24 875            | 13 896          | 48 201    | 65 496         | 84 196      | 236 665           | 8                           | 273 979             | 231 915    | 87 481              | 830 040     | 1.91   |
| Cyprus         | 1068              | 2808            | 765       | 4540           | 24 773      | 33 955            | 3                           | 56 585              | 6601       | 23 941              | 121 082     | 0.68   |
| Czech Republic | 32 018            | 78 366          | 15 129    | 278 463        | 229 354     | 633 331           | 6                           | 523 448             | 236 458    | 181 275             | 1 574 512   | 1.03   |
| Denmark        | 6899              | 56 498          | 7855      | 299 211        | 234 398     | 604 861           | 2                           | 1 167 468           | 396 098    | 737 586             | 2 906 014   | 1.18   |
| Estonia        | 7988              | 14 579          | 6973      | 31 623         | 11 905      | 73 067            | 7                           | 64 522              | 39 182     | 21 156              | 197 928     | 1.14   |
| Finland        | 38 094            | 190 986         | 27 561    | 535 402        | 179 297     | 971 340           | 6                           | 640 870             | 106 867    | 314 278             | 2 033 355   | 1.06   |
| France         | 118 410           | 187 718         | 22 806    | 4 681 469      | 3 462 372   | 8 472 775         | 4                           | 6 221 407           | 2 796 025  | 3 040 203           | 20 530 410  | 1.01   |
| Germany        | 1 316 014         | 1 082 986       | 22 925    | 9 824 295      | 2 732 580   | 14 978 799        | 5                           | 12 802 215          | 2 250 307  | 4 734 815           | 34 766 136  | 1.30   |
| Greece         | 58 052            | 129 744         | 25 670    | 534 413        | 329 836     | 1 077 715         | 6                           | 622 867             | 72 683     | 318 728             | 2 091 994   | 1.08   |
| Hungary        | 38 753            | 60 049          | 10 006    | 251 296        | 253 159     | 613 264           | 8                           | 460 174             | 72 588     | 168 948             | 1 314 973   | 1.36   |
| Ireland        | 32 269            | 33 694          | 17 804    | 400 357        | 145 071     | 629 196           | 4                           | 571 817             | 102 212    | 175 213             | 1 478 437   | 0.90   |
| Italy          | 537 037           | 600 712         | 401 205   | 3 870 315      | 1 904 371   | 7 313 639         | 5                           | 5 081 057           | 169 699    | 4 820 340           | 17 384 735  | 1.11   |
| Latvia         | 6436              | 14 880          | 1306      | 27 441         | 12 711      | 62 774            | 5                           | 99 810              | 21 721     | 30 597              | 214 903     | 0.97   |
| Lithuania      | 8963              | 8780            | 2581      | 31 449         | 9938        | 61 711            | 3                           | 115 910             | 39 712     | 31 261              | 248 594     | 0.75   |
| Luxembourg     | 4582              | 8293            | 627       | 59 746         | 29 439      | 102 687           | 4                           | 60 723              | 41 319     | 30 120              | 234 849     | 0.55   |
| Malta          | 817               | 1348            | 498       | 7714           | 9884        | 20 260            | 3                           | 14 080              | 1165       | 11 140              | 46 646      | 0.68   |
| Netherlands    | 126 000           | 193 079         | 16 798    | 2 174 600      | 288 905     | 2 799 382         | 4                           | 2 781 602           | 557 599    | 912 671             | 7 051 254   | 1.18   |
| Poland         | 101 656           | 314 960         | 11 630    | 513 845        | 298 155     | 1 240 246         | 5                           | 1 597 574           | 533 564    | 561 867             | 3 933 251   | 1.03   |
| Portugal       | 71 473            | 118 014         | 29 372    | 141 055        | 282 337     | 642 252           | 4                           | 1 058 365           | 91 259     | 351 235             | 2 143 112   | 1.30   |
| Romania        | 20 546            | 68 199          | 3134      | 158 524        | 222 534     | 472 937           | 9                           | 803 769             | 119 766    | 152 038             | 1 548 509   | 1.18   |
| Slovakia       | 34 599            | 84 097          | 4235      | 96 639         | 127 683     | 347 254           | 6                           | 202 230             | 112 862    | 67 765              | 730 111     | 1.03   |
| Slovenia       | 3952              | 8356            | 5400      | 91 949         | 53 555      | 163 212           | 5                           | 154 566             | 126 916    | 73 538              | 518 232     | 1.47   |
| Spain          | 864 251           | 504 313         | 290 529   | 2 141 670      | 1 734 181   | 5 534 944         | 6                           | 3 205 636           | 534 071    | 2 373 813           | 11 648 464  | 1.13   |
| Sweden         | 71 174            | 233 559         | 55 198    | 721 068        | 313 295     | 1 394 294         | 4                           | 1 062 042           | 513 982    | 533 911             | 3 504 229   | 0.86   |
| United Kingdom | 194 945           | 1 377 068       | 56 558    | 3 313 326      | 1 336 878   | 6 278 775         | 3                           | 8 095 221           | 1 386 307  | 3 130 825           | 18 891 128  | 0.98   |
| TOTAL EU       | 3 801 513         | 5 528 713       | 1 120 266 | 31 857 045     | 15 149 973  | 57 457 509        | 5                           | 50 223 799          | 11 755 588 | 23 912 240          | 143 349 138 | 1.11   |

A&amp;E = accident and emergency; EU = European Union; GDP = gross domestic product.



with bladder cancer accounting for 3%. In Greece, Italy, Malta, and Spain, bladder cancer represented >4% of all total cancer costs, whereas in Ireland, the country with the lowest proportion, bladder cancer accounted for approximately 2% of total costs.

The health care cost of cancer was €57 billion (Table 3), with bladder cancer representing 5% of these costs. In Italy, bladder cancer accounted for 7% of total cancer care costs, whereas in Hungary and Ireland, it accounted for <3%. Figure 2 and Supplementary Figure 2 report the per capita

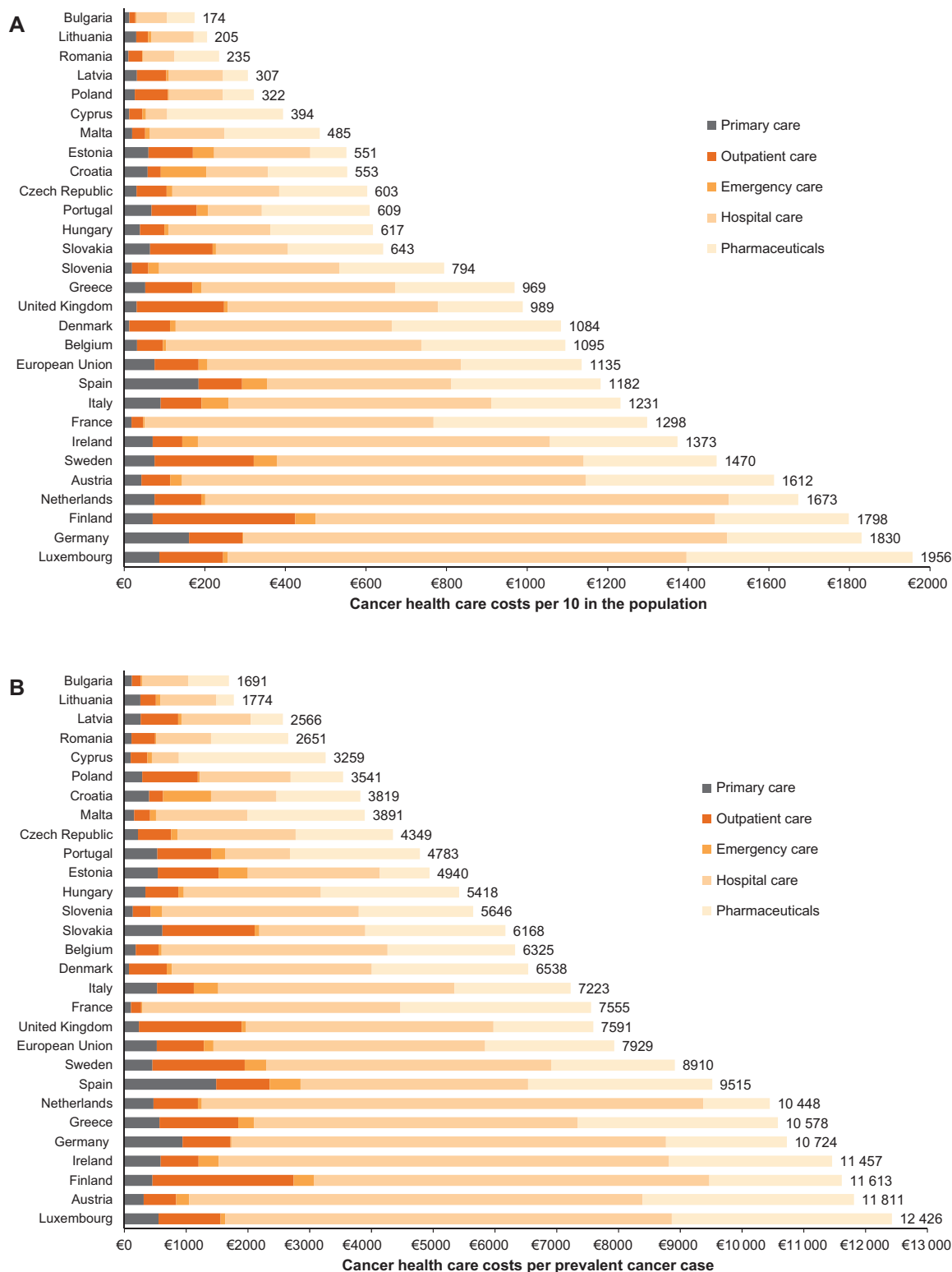


Fig. 2 – Total health care costs (€), not adjusted for price differentials, of cancer by health care service category (A) per 10 in the population, 2012, and (B) per prevalent cancer case.

health care costs attributable to overall cancer unadjusted and adjusted for price differentials, respectively.

#### 4. Discussion

We estimated the total costs of bladder cancer to be €4.9 billion in 2012 across the EU. To our knowledge this is the first study to provide estimates of the economic burden of bladder cancer in the EU.

The annual health care expenditures due to bladder cancer accounted for €57 per 10 EU citizens or €6942 per prevalent case. The largest component of health care costs was inpatient care (€1.7 billion [58%]) followed by the costs of medicines (€0.6 billion [20%]). In the United States, inpatient and outpatient costs of bladder cancer were estimated at €3.2 billion in 2010 [16], which amounts to twice the expenditure per 10 US citizens relative to the EU (€97 PPP in the United States vs €45 in EU), after adjusting for price differentials. A similar ratio was found when health care costs were estimated per prevalent case, adjusting for price differentials.

Some suggest [17] that this higher expenditure on bladder cancer might explain the lower age-adjusted MIR in the United States relative to the EU-28 countries as a whole (0.21 vs 0.27 deaths per incident case in 2012). However, when US mortality statistics are compared with European countries with similarly high national incomes, these differences disappear (eg, 0.15 in Germany, 0.34 in France, and 0.23 deaths per incident case in Sweden) [2]. As a result, some researchers have questioned the effectiveness of higher US spending and suggested it is driven by higher costs, unnecessary testing, and unproven medical procedures [18]. The debate continues on whether higher spending in the United States results in better cancer outcomes [19] and how these can be best measured [20].

Large variations in bladder cancer health care costs were also found between European countries, ranging from €8 per 10 in the population in Latvia to €94 per 10 in the population in Luxembourg. Although these differences narrowed after adjusting for price differentials across countries, important differences persisted. In our analysis, the most important predictor of bladder-related health care costs was per capita national income, which explained higher unit costs in richer countries. For example, according to Eurostat, average annual salaries in human health and social work activities in Bulgaria were €4660 as opposed to €35 434 in Sweden, which could explain the large differences in the unit costs (eg, in Bulgaria a visit to a specialist was found to cost €20 as opposed to >€300 in Sweden).

However, even for countries with the same levels of wealth, health care costs on bladder cancer varied widely. For example, even though France and the United Kingdom have similar levels of per capita gross domestic product, France's expenditure on bladder cancer-specific health care was considerably higher than that of the United Kingdom. Differences in health care expenditures due to bladder cancer could be explained by health system configuration (eg, the number of hospital bed days due to bladder cancer

in Germany is substantially higher than in Sweden). Substantial variations in pharmaceutical expenditure could also be explained by a myriad of factors such as differences in the introduction and use of new drugs, differences in the prices paid for the same drugs, increased pharmaceutical consumption in some countries; differences in the types of medication consumed, different price setting and reimbursement mechanisms, or variations in clinical practice. The patterns explaining the between-country differences in bladder cancer expenditure should be researched further.

It is then important to identify the most efficient public policy initiatives and health care systems capable of achieving the best cancer outcomes so that benchmarks can be set up across the EU member states. More research is thus required on factors affecting access to treatment and diagnosis and on biologic differences so that gender differences in the incidence and mortality of bladder cancer across the EU can be explained [21]. More EU research is needed to address intelligence gaps concerning the effectiveness and cost effectiveness of existing management and surveillance technologies for bladder cancer so that best practices can be based on robust evidence [22].

Bladder cancer contributed to 3% of the total cancer costs (€143 billion) in the EU in 2012. Luengo-Fernandez et al (2013) [1] found that of the total economic cost of cancer in 2009, 44% was due to lung (15%), breast (12%), colorectal (10%), and prostate cancers (7%). Of total health care cancer costs in 2009, prostate cancer accounted for 11%, which is considerably higher than that identified in this study for bladder cancer (5%). However, according to the IARC, the prevalence of prostate cancer is three times higher than that of bladder cancer in the EU [2], suggesting that the health care cost per prevalent cancer is higher for bladder than prostate cancer. Using the same methodology and sources as that used for the 2009 analysis, we estimated that the cost per prevalent bladder cancer was €5621 in 2009 compared with €4282 for prostate cancer. These findings are supported by research in 2011 estimating health care costs of bladder cancer per patient to be higher than prostate cancer across all disease phases [16].

Cost-of-illness data describe the magnitude of public health problems and allow comparisons across different types of cancers, diseases, and countries. If performed consistently over long periods of time, these types of analyses will aid prioritising health care resources and research funding towards diseases with the highest burden, identify the largest components of costs (eg, inpatient services), and provide valuable data to support economic evaluations of health care technologies. They can also provide evidence to assess whether at the population level, cancer care policies, such as increases in pharmaceutical expenditure, cost containment plans, and screening programmes, are translated into changes in cancer-specific health care costs, which then in turn can be evaluated against changes in outcome or non-health care cancer costs. Hence such data can aid decisions about the allocation of EU resources including service provision, prevention strategies, and future research funding [23].



We estimated the costs of cancer to increase from €126 billion to €143 billion between 2009 and 2012 across the EU-27 countries included in both analyses. According to the IARC and Eurostat, cancer incidence and mortality increased by 7% and 2%, respectively, in the same period. This translated into the number of working-years lost due to premature death increasing by 7.4 million years and days lost due to absence from work increasing by 2.1 million. These, together with changes in employment rates and wages, led to an increase in lost earnings due to cancer-related early death and absence from work of 18% (€9.5 million). In terms of health care resource use, a decrease was observed across most care categories. For example, reported cancer-related inpatient days were 8% (4.6 million days) lower in 2012 relative to 2009, without any discernible increase in informal care costs (€23.2 billion in 2009 vs €23.9 billion in 2012). However, the reduction in cancer-related health care resource use was counterbalanced by a significant rise in health care price inflation and the introduction of newer and more costly technologies that resulted in an overall increase in health care costs of €5.9 billion (12%).

This analysis has limitations. Despite the need to improve and standardise disease and resource use data across the EU [24], this remained largely unchanged between 2009 and 2012. For example, we used >150 sources for this study, and with the exception of inpatient days, national data were largely absent on the number of primary care, outpatient care, and A&E visits due to cancers and bladder cancer, requiring assumptions and extrapolations to estimate these. We provide a grading system here for each resource use and unit cost used regarding the quality of the sources available (Supplementary Table 1 and 2). Due to data availability, we did not consider other types of drugs, such as antiemetic drugs. We also found a lack of detailed prospective studies of cancer patients and national linked databases ascertaining medication expenditure by type of cancer and disease phase. As a result, the proportion of country-specific cancer-related pharmaceutical expenditures due to bladder cancer medication was ascertained using estimates from two countries (Germany and the Netherlands), which were then applied to the remaining countries. However, a sensitivity analysis showed alternative assumptions to result in changes of only 5% on total bladder cancer costs. Finally, our absolute costs are likely to be an underestimate. Some categories of health care costs, such as public health activities and screening programmes, long-term morbidities resulting from cancer treatments amongst survivors, and care provided outside the health care system (eg, hospices based outside hospitals), is not recorded for all countries under study. However, the estimates of the proportion of total cancer costs that were due to bladder cancer are less likely to be affected because these were also missing across all cancers.

## 5. Conclusions

Our study is the first to quantify the economic burden of bladder cancer in the EU and its contribution to total cancer

costs. Urologic services are key cancer-specific pathways in EU countries, and bladder cancer makes up a significant burden on these systems. We believe that our study will be of particular interest to European policymakers implementing affordable cancer care for all European citizens. Our study updates and adds cost data to inform evidence-based policy making.

**Author contributions:** Ramon Luengo-Fernandez had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

**Study concept and design:** Leal, Luengo-Fernandez.

**Acquisition of data:** Leal, Luengo-Fernandez.

**Analysis and interpretation of data:** Leal, Luengo-Fernandez.

**Drafting of the manuscript:** Leal, Luengo-Fernandez, Sullivan, Witjes.

**Critical revision of the manuscript for important intellectual content:** Leal, Luengo-Fernandez, Sullivan, Witjes.

**Statistical analysis:** Leal, Luengo-Fernandez.

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## Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at <http://dx.doi.org/10.1016/j.eururo.2015.10.024>.

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