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The burden of healthcare costs associated with prostate cancer in Ireland

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ABSTRACT

Purpose: With one of the highest incidences across Europe and the rest of the World in 2012, the Republic of Ireland (RoI) has experienced significant increases in prostate cancer (PCa) since 1994. The main driver is the widespread use of PSA testing which is used to detect PCa. This is expected to have significant implications on resource use in the RoI. The focus of this paper was to (i) derive costs for the PCa pathway, from diagnosis to treatment, and (ii) estimate overall healthcare expenditure for PCa in the RoI.
Methods: PCa incidence (ICD-10 code: C61), treatment and mortality data during 2007-2010 was obtained from the National Cancer Registry Ireland. Costs associated with diagnosis, treatment, treatment complications, clinical follow-up to year four post-diagnosis and terminal (palliative) care were estimated using sources such as survey data, Irish inpatient costs and published costs.
Results: The overall estimated burden of healthcare costs associated with those diagnosed with PCa and receiving care (up to four-year post-diagnosis) or dying from PCa in 2010 was approximately €45.6 million. The overall cost associated with detection, via PSA testing, for those diagnosed with PCa in 2010 (n = 3287) was €366,369. Treatment costs varied considerably with the most expensive treatment being chemotherapy and radical prostatectomy (unit cost €11,278 and €7324, respectively).
Conclusions: PCa incidence partly due to high levels of PSA testing has significant resource utilisation implications in the RoI.

Keywords: Costs, Detection, Prostate cancer, PSA testing, Treatment

Introduction

Over the last two decades, in many Western countries, the incidence of prostate cancer (PCa) has been rising. It is the second most common cancer in men Worldwide (1), with an estimated 1.1 million men diagnosed in 2012 (2). PCa also imposes a significant economic burden on society with an estimated cost of €8.4 billion to the European Union in 2009, 7% of all cancer costs (3). Trends in PCa incidence in Ireland and elsewhere are thought to be largely explained by the increased rates of prostate specific antigen (PSA) testing among asymptomatic men (4-7). Although the European Randomised Study of Screening for Prostate Cancer (ERSPC) reported a 21% reduction of cancer-related death due to PSA screening compared to no screening (5), these benefits must be balanced against the harmful consequences of over-diagnosis and overtreatment of PCa (8-10). In comparison, the US PLCO trial found no such evidence of mortality reduction at 13 years' follow-up (11). The consequences of over-detection and over-diagnosis are of significant concern because not all PCas would have become clinically apparent within their lifetime; estimates of the pool of PCas susceptible to over-detection vary from 1%-2% in men aged 20-29 years to 59%-72% in men aged 90-99 years (12). Furthermore, the recent results of the ProtecT randomised trial on detection and treatment for PCa suggests that there is no significant difference between Active Monitoring (AM) and more radical treatment modalities in prostate-cancer-specific mortality (13).

The Republic of Ireland (RoI) has one of the highest PCa rates in Europe and the fourth highest rate in the world

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(14, 15); this is largely due in part to the fact that population coverage of PSA testing is considered higher than in most other European countries (6, 16, 17). The annual cost of PSA testing alone in the RoI was estimated to be €3.6 million in 2010 (18). However, the total economic impact of PCa in the RoI is unknown and its estimation is challenging due to the complexity of the healthcare delivery model (mixed public/private model) (19) and the limitations of published reference costs (20). PCa-related costs vary across payers, thus providing further obstacles in estimating healthcare costs across all payer types (20). Due to the steady increases in PCa in the RoI since 1994 and current projections for growth, it is important to understand the economic impact in order to assess both the drivers of cost and the potential for cost-containment strategies.

The aim of this analysis was two-fold: first, we estimated resource use associated with the different components of PCa healthcare in the RoI including detection, diagnosis, treatments and follow-up care, which has not been undertaken previously; second, combining these with unit costs, we estimated the overall healthcare expenditure for PCa in 2010.

Methods

Data, treatment pathways and healthcare utilisation

Details of PCa (ICD-10 code: C61) cases diagnosed during 2007-2010 were obtained from the population-based National Cancer Registry Ireland (NCRI). Deaths from PCa and other causes during 2007-2010 were obtained from the Central Statistics Office (CSO) via the NCRI and linked to incident cases. Patient clinical, diagnostic and treatment data were extracted from the NCRI database for the period 2007-2009. A PCa patient pathway was constructed based on available NCRI data, the most up-to-date literature (21-23), and expert clinical opinion (24).[1] Healthcare utilisation associated with each step of the pathway was derived from the NCRI database, a patient survey administered by the NCRI (25) and a recent HTA appraisal of PSA testing (26) (Tab. I). PCa detection was assumed to include two GP visits and two PSA tests prior to biopsy referral based on clinical (24) and national guidance (27) for Ireland. From survey responses, men were assumed to have had, on average, 1.25 biopsies (25); this was verified by clinical expert opinion (24). Rates of severe complications of biopsy, including infection and hospitalisation were sourced from the HTA of PSA testing for the detection of PCa (26). These data were for the UK; no relevant data are available for Ireland.

Treatments and procedures recorded by the NCRI for the first year of diagnosis included biopsies, radical prostatectomy (RP), external beam radiation therapy (EBRT), brachytherapy (BT), other surgery (transurethral resection of the prostate [TURP]), hormone therapy (HT), chemotherapy (CT), active monitoring (active surveillance or watchful waiting [AM], which cannot be distinguished in NCRI data) and combinations thereof. The allocation of treatments at PCa diagnosis was estimated by averaging the national PCa treatment data over 2007-2009. EBRT was assumed to be intensity-modulated radiation therapy (IMRT) and HT was assumed to be goserelin. Components of AM were based on expert opinion (24) and included four GP visits per year each including a PSA test, one

TABLE I - Resource use parameters

Treatment/diagnosis parameters[a]	Average utilisation	Sources
Post-biopsy MRI	30% (25%-35%)	NCRI data 2014[b] (patient reported survey)
Post-biopsy bone scan	30% (25%-35%)	NCRI data 2014[b] (patient reported survey)
Post-biopsy complication rate	1.4% (1%-3%)	Hummel et al 2013 (26)
Repeat biopsy rate	1.25% (1.10%-1.40%)	NCRI data 2014[b] (patient reported survey)
Active monitoring (AS/WW)	20%	NCRI data (2007-2009)[c]
Surgery - radical prostatectomy	15%	NCRI data (2007-2009)[c]
Surgery - TURP	14%	NCRI data (2007-2009)[c]
External beam radiation (IMRT)	40%	NCRI data (2007-2009)[c]
Brachytherapy	4%	NCRI data (2007-2009)[c]
Hormone therapy - goserelin	31%	NCRI data (2007-2009)[c]
Chemotherapy - docetaxel and prednisolone	2%	NCRI data (2007-2009)[c]

[a] Treatments are not mutually exclusive as some patients received multiple treatments.
[b] Project-specific survey data unpublished to date but described in Drummond et al (2015) (25).
[c] The National Cancer Registry database was used to estimate the proportions of PCa patients receiving the different treatment modalities; the NCRI captures approximately 96% of all cancers in the Republic of Ireland (45).
MRI = magnetic resonance imaging; AS/WW = active surveillance/watchful waiting; TURP = transurethral resection of the prostate; IMRT = intensity modulated radiation therapy; PCa = prostate cancer; NCRI = National Cancer Registry Ireland.

[1] Members of the Department of Radiology, University College Hospital, Galway, including author Professor Frank Sullivan provided guidance on the clinical pathways and undertook a micro-costing analysis which informed cost components of this analysis. This costing analysis has not been published to date.

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out-patient appointment per year and one biopsy per year (27). Post-treatment follow-up included medication, GP and out-patient attendance (22, 23, 27), other surgical procedure and diagnostic tests (22, 23, 26, 28-30), and were assumed to continue for three years after the first year of diagnosis; these assumptions were based on a synthesis of the literature and expert clinical opinion (24). Terminal (palliative) care included medication (30, 31), diagnostic treatment and end-of-life care based on an average length of stay of 13 days in an inpatient setting in Ireland (20).

Treatment complications were categorised into short term (<1-year post-treatment). and long term (>1-year post-treatment) and included incontinence (23), impotence (23), risk of cardiovascular disease (CVD) (30) and risk of fracture (32); based on published sources, these were assumed to vary by treatment modality (26-29). Consequences of complications were assumed to be hospitalisation, further diagnostic tests and treatments (33).

Unit costs

The perspective of this analysis was that of the public payer. Hence, only direct healthcare costs were included. Costs were estimated by multiplying cancer-related contacts/resource utilisation by the respective unit costs. The unit costs associated with diagnosis, treatment, treatment complications (short- and long-term) and terminal care were obtained from survey data (18, 34), Irish (35), and UK reference costs (36) and previously published sources (20, 23, 31) (Supplementary Table I, available online at www.grhta.com). Medication costs, including HT costs, were sourced from the HSE Primary Care Reimbursement Service database and with the assistance of a community-care pharmacist (37). Costs of detection were calculated using project-specific survey instruments described in detail elsewhere (18, 34). Costs of EBRT and BT were sourced from an ongoing micro-costing analysis undertaken by an Irish hospital (24). All costs were expressed in 2010 (€) using standard methods of inflation recommended by Irish guidelines (HIQA & CSO) (38) and non-Irish costs were adjusted using the purchasing power parity (PPP) method (39).

Analysis

Incident cases (2007-2010) were broken down by year, age group and clinical stage at diagnosis (Supplementary Table II, available online at www.grhta.com). Full clinical and treatment data on all PCa cases diagnosed in 2010 were unavailable at the time of analysis, so the stage and treatment distribution was based on 2007-2009 data. The healthcare costs of PCa were estimated using two approaches: incidence-based (IB) and prevalence-based (PB); this was for purposes of comparison. The IB approach consisted of estimating solely the annual costs of those patients diagnosed in 2010 (n = 3287), whereas the PB approach consisted of estimating the costs of all men with PCa in 2010 regardless of the year of disease onset. The PB approach assumed that after four years' post-diagnosis no further management would be necessary and hence, no PCa-related costs would occur. Therefore, to estimate overall costs, the costs for patients diagnosed in 2010 (IB) were combined with costs of patients diagnosed between 2007 and 2009 who were alive at the beginning of 2010 (PB) (n = 11,054). and terminal (palliative) costs for men who died from PCa in 2010 (n = 533). Both approaches involved estimating costs of resources used at the patient level, i.e., consistent with a bottom-up approach. Since several management options are available for patients with localised disease, scenario analysis was performed to investigate the impact on total cost of reallocating patients from more- to less-costly treatment regimens for this clinical subgroup, i.e., increasing proportions treated by AM or BT instead of RP and EBRT. HT and CT were not adjusted as these strategies for treatment/management of PCa are used in more advanced stages and therefore have limited treatment alternatives.

TABLE II - Healthcare costs of prostate cancer in Republic of Ireland, in 2010 (€ millions)

	Incident costs (IB approach)	Prevalent costs (PB approach)
Men with PCa in 2010	3287	11,054
Men with PCa who died in 2010	185[a]	533[b]
Detection of PCa	€0.37 million	€ 0.37 million
Diagnosis of PCa (including biopsy complications)	€ 3.05 million	€ 3.05 million
Treatment and clinical follow up	€ 20.81 million	€ 33.84 million
Treatment related complications	€ 0.64 million	€ 4.79 million
Terminal care	€ 0.91 million	€ 3.71 million
Total costs	€ 25.7 million	€ 45.6 million
Average cost per PCa diagnosis (with complications)	€7532	€13,818
Average cost per PCa diagnosis (without complications)	€7337	€12,360

[a] The number of men diagnosed with PCa in 2010 and died within the 12 months.
[b] The number of men diagnosed with PCa from 2007-2010 and died in 2010.
PCa = prostate cancer; IB = incidence based; PB = prevalence based.

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Results

Table II shows the healthcare costs in RoI associated with PCa in 2010 for both approaches. In 2010, the overall cost associated with PCa detection (n = 3287) was €366,369. PCa diagnosis, which included biopsies (€432/patient) and diagnostic procedures (€376/patient), was estimated at €3 million (unit cost [UC] €808). The healthcare cost per patient, in 2010, for the first year of PCa diagnosis was estimated at €7337, excluding treatment complications, or €7532, including treatment complications. Estimated treatment costs (for the first year) varied considerably; AM €430,572 (UC €655), EBRT €8.05 million (UC €6122), RP €3.6 million (UC €7324), BT €591,496 (UC €4999), TURP €2.6 million (UC €5709), HT €4.8 million (UC €4670), and CT €741,404 (UC €11,278). Post-treatment costs, which included three years' follow-up after the first year of diagnosis for patients diagnosed 2007-2009, but still treated in 2010, were estimated at €13 million. Costs associated with treatment complications were estimated at €4.8 million. The cost associated with terminal care for the 533 PCa deaths in 2010, of which 185 (35%) were due to cancers diagnosed in that year, was estimated at €3.7 million (UC €6958).

In 2010, the total healthcare costs associated with PCa (up to four years' post-diagnosis), i.e., employing the PB approach, was approximately €45.6 million. The healthcare cost from PCa diagnosis up to four years' post-diagnosis, including biopsy and treatment complications, was estimated at €13,818 per patient. The total estimated burden of newly diagnosed PCa in 2010, i.e., adopting the IB approach, was approximately €25.7 million.

PSA testing in cancer patients accounts for the smallest proportion of costs for both the IB and PB approaches; 1.4% and 0.8%, respectively. HT was delivered both in isolation and in combination with radical treatments and represented the largest proportion of the PB total costs (32%). EBRT and BT combined accounted for the 34% and 22% of costs in IB and PB approaches, respectively. Also, EBRT accounted for the highest proportion of costs in newly diagnosed cases (IB approach). RP, although only administered to 15% of patients, represented 14% and 9% of the total costs in the IB and PB approaches, respectively.

Scenario analyses are shown in Table III. Redistributing localised cancers from costlier treatments (RP (-10%) and EBRT (-15%) to BT (+15%) and AM (+10%) has a marginal impact on the overall burden of cost in all scenarios, a maximum reduction of €3.2 million (7%).

TABLE III - Treatment scenario analyses for prevalent costs in 2010

Utilisation of treatments	Base-case	Scenario 1	Scenario 2	Scenario 3
AM	20.0%	30.0%	30.0%	30.0%
RP	15.0%	10.0%	5.0%	5.0%
EBRT	40.0%	35.0%	30.0%	25.0%
BT	3.6%	3.6%	13.6%	18.6%
HT	31.0%	31.0%	31.0%	31.0%
CT	2.0%	2.0%	2.0%	2.0%
Total cost (€ million). (PB)	€45.6	€43.4	€42.6	€42.4
Reduction in cost relative to base-case analysis [€ million] (%)		€2.2 (4.8%)	€3.0 (6.6%)	€3.2 (7.0%)

Discussion

In this study, we estimated costs and resource utilisation rates for PCa diagnosis and treatment in the RoI in 2010 using available Irish data. Total PCa healthcare expenditure was estimated at €45.6 million, equating to 0.027% of Ireland's GDP and 0.32% of public expenditure on healthcare in 2010 (40); this is similar to % of GDP attributable to PCa in the UK (0.024%) and lower than that of France, Italy and Sweden (0.049%, 0.038% and 0.039%, respectively) (3). Clinical stage at diagnosis and variation in treatment modalities may in part account for variation across countries. However, with growing pressures on healthcare budgets, an aging population and steady growth in PCa incidence, driven in part by increased PSA testing in primary care and longer life expectancy, understanding the components of the burden of cost and how they compare with European counterparts is vital for constructing policy responses. As expected, PCa treatment regimens accounted for most of costs (€34 million, 74%); however, short- and long-term complications post-treatment also constituted a significant burden (€4.8 million, 11%). Furthermore, we estimated that over half the PCa expenditure was attributable to diagnosis and first year of treatment (€25 million). Using incidence data, the diagnosis and treatment of PCa in the RoI was estimated at €7337 (2010€) per patient excluding treatment complications. Incidence costs of PCa in the UK of €3682 (2006€), Germany €3698 (2006€), Spain €3256 (2006€), Italy €5226 (2006€) and France €5851 (2006€) were comparable after adjusting for PPP (41). The cost of €13,818 per prevalent case (including four years' follow-up) in the RoI is similar to the cost of €12,731 in France (2008€ including five years' follow-up) (42). However, costs of PCa care in the RoI are among the highest in Europe.

A European study estimated that across Europe the total cost of cancer in 2009 was €126 billion and the annual Irish direct healthcare cost of PCa in 2009 was €51 million. The study adopted a top-down approach using national fee schedules and expenditure data incorporating public and private healthcare expenditure (3). Our estimates included public payer costs only, which may account, in part, for the discrepancy between estimates. Previous research found that approximately 30% of men diagnosed with PCa used private healthcare providers (43). The unit costs used in our study for this sub-group may be conservative, as costs of treatments in the private setting are thought to be substantially higher than the public system; however, there are no data available on the unit cost differences across the two modes of healthcare delivery within the RoI. If adopting a 15% adjustment for private care in Ireland applied in Luengo-Fernandez et al (3) to the proportion treated privately (approximately 30%) (43), this would increase the total cost of PCa in the RoI to €47.7 million.

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The scenario analysis highlighted that potential annual savings ranging from €2.2 million to €3.2 million are possible if suitable patients with localised disease received less costly management options, namely AM and BT. Between 2007 and 2009, approximately 65% of PCa was diagnosed as localised disease (Stage I-II). Those receiving AM and BT accounted for 24% on average and those in receipt of RP and EBRT accounted for 55%. Whether greater use of AM or BT is clinically justified and aligns with European guidance needs further investigation (44). However, the ProtecT trial findings (13), suggest there is no mortality benefit for treating patients with localised PCa with more aggressive, costlier treatment modalities over a 10-year follow-up period; thus, suggesting redistribution of care to AM, in particular, may be a viable cost-containment strategy. Monitoring of trends in treatment and examination of practice variation is warranted.

This study has several limitations. Resource use estimates for post-biopsy complication rates were informed by published studies as data were not available in the RoI. For HT, we assumed goserelin was solely used and for CT we assumed docetaxel in combination with prednisolone was solely used; both assumptions were made due to limited treatment data available in the RoI and we acknowledge that other products are prescribed in the RoI. In the absence of published data in the RoI, sources from UK studies as well as expert opinion have informed the resource use parameters and costs associated with some elements of treatment. Other parameters were sourced from relevant literature, which focussed primarily on identifying data from the UK (as another public healthcare system); if UK data could not be identified, data from other countries was used. Although, our aim was to estimate all Irish costs using a bottom-up approach based on patient level data, this was not possible for all elements of care given the lack of data and resources to perform micro-costing exercises. For example, treatment unit costs were retrieved from the readily available HSE Casemix programme database which reports costs by diagnosis-related groups (gross costing where patients are grouped according to similar levels of resource usage), rather than using a micro-costing approach to collect and value all resources associated with all treatments. Thus, it could be argued that not all costs estimated in our study are fully consistent with a bottom-up approach. A more apt classification is a mixture of bottom-up and top-down (gross-costing) approach that was conditional on the availability of data.

Finally, this analysis captured expenditures associated with PCa for those diagnosed and registered with the NCRI. However, registry completeness, although high, is not 100% (45). Moreover, based on UK trial data, approximately 9% of those screened have a raised PSA (defined as >3 ng/mL) and 23% of those 9% are diagnosed with PCa (46). Applying these proportions to the RoI suggests that the 3287 diagnosed in 2010 may only represent 23% of the men who underwent a biopsy after an abnormal PSA test. However, previous research suggests that approximately 17% of those tested had an abnormal PSA test in the RoI, nearly double the rates of the ProtecT trial (6); further, biopsy rates for suspected PCa in the RoI are considerably higher than in the UK (47). Thus, extra PCa-related expenditure associated with PSA testing and biopsies for those who did not have PCa could range between €1.5 million to €3 million; these costs were not included in our estimates but may account for the cost difference presented here and that of the Luengo-Fernandez et al study (3).

Conclusion

The estimated burden of cost associated with PCa in the RoI for 2010 was €45.6 million employing a public payer's perspective. Healthcare expenditures associated with PCa are substantial representing a sizeable proportion of the Irish healthcare budget in relation to disease prevalence. Increases in PCa incidence, in part due to PSA testing, have significant resource utilisation implications in the RoI as well as across Europe; this study aids in understanding the PCa pathway and associated costs in the RoI which may highlight areas of focus for cost containment strategies.

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