CARDI GRANTS PROGRAMME

Research Brief

Is age a determining factor in the treatment of men with prostate cancer?

Ageing population: ROI

- At the 2006 census, there were 468,000 people aged 65+ (11% of the population).
- By 2041, there will be 1.4 million aged 65 and over (22% of the population).
- Life expectancy is 76.8 years for men and 81.6 years for women.
- 95% of men and women aged 70 and over rate their health as very good (19%), good (50%) or fair (26%).
- 9.1% of people aged 65 and over are still in employment (Q2 2009).

Ageing population: NI

- In 2010, there were 260,000 people aged 65+ (14% of the population).
- The 65+ age group will be 496,000 in 2041 (24% of the population) and 578,000 in 2061 (28% of the population).
- Life expectancy is 77 years for men and 81.4 years for women.
- 66% of people aged 70 and over rate their health as good (25%) or fairly good (42%).
- 9% of men aged 65 and women aged 60+ are still in employment (Q2 2009).

Policy on cancer: RoI

- In RoI the Cancer Policy Unit (CPU) is responsible for developing legislation and policy to support a national cancer control system. Among other things it supports the Health Service Executive (HSE) to ensure the implementation of policy and the effective delivery of cancer services.

- The National Cancer Control Programme July 2011 provides for the establishment of Rapid Access Diagnostic Clinics for prostate cancer in six of the eight national cancer centres.

Policy on cancer: NI

- The NI Health Minister launched the Service Framework for Cancer Prevention, Treatment and Care in February 2011. It sets out standards for cancer services on the prevention, diagnosis, treatment, ongoing care, rehabilitation, and palliative and end of life care. The framework includes overarching standard 45: 'Radical surgery for prostate and bladder cancer should be provided by teams carrying out a total of at least 50 such operations per annum and should take place on a single site, which offers appropriate post-operative care'.

Introduction

Prostate cancer is the most common cancer among men on the island of Ireland (Donnelly, Gavin et al., 2009), accounting for a quarter of all male cancers. Its incidence has been increasing in recent decades in Northern Ireland (NI) and even more so in the Republic of Ireland (RoI). Thanks to improved treatment, the death rate for men with prostate cancer is declining, but it still accounted for 766 deaths in the whole of Ireland in 2010.

A particular feature of prostate cancer is that it is common among older men. Since the number of older men will almost triple over the next 30 years, there is the prospect of prostate cancer becoming even more prevalent than it is now. There is also evidence of differences in the treatment of younger and older men.

To investigate this issue, CARDI awarded a grant in November 2009 to the Northern Ireland Cancer Registry (NICR), Queen's University Belfast, for an investigation of treatment variations in prostate cancer in Northern Ireland and the Republic of Ireland. This research brief draws on the final research report 'Is age a determining factor in the treatment of men with prostate cancer?' (Donnelly et al., 2012) and on other material compiled by CARDI.

Key findings

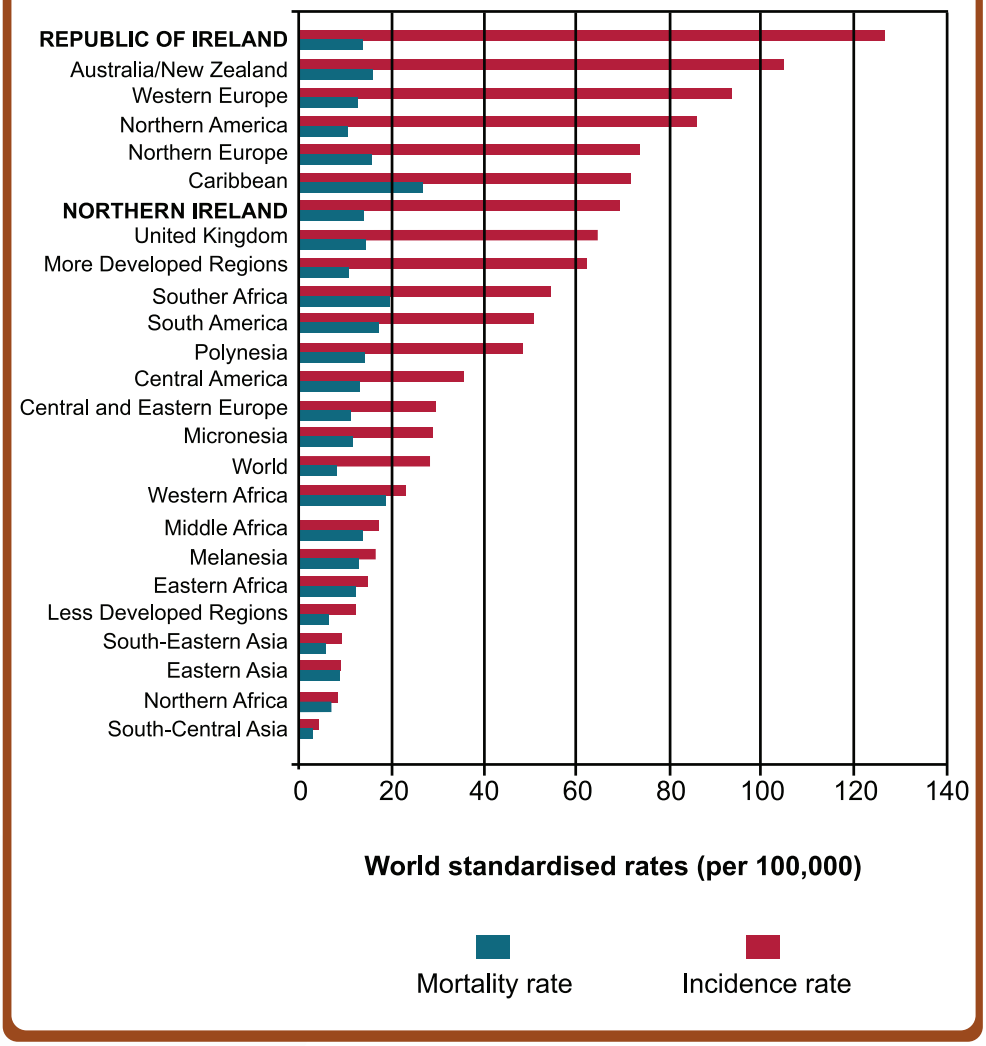
- Prostate cancer is the most common cancer among men on the island of Ireland, comprising one quarter of all male cancers.
- In 2010, 766 people died of prostate cancer, 521 in RoI and 245 in NI. However survival rates from prostate cancer have risen from about 60% to over 80%, reflecting increased diagnosis of early stage disease.
- The rate of prostate cancer among men aged 70+ is 12 times higher than for younger men and death rates are 74 times higher.
- Rates of prostate cancer are very high by international standards, especially in RoI, where rates are increasing faster than for any other common cancers (Donnelly, Gavin et al., 2009). In part this is because more cases are being picked up by increased Prostate Specific Antigen (PSA) testing.
- Men aged 70+ are 22% less likely than younger men to see a urologist and far less likely to have radical prostatectomy or radiotherapy. Treatment may reflect clinical conditions of older men e.g. the presence of other diseases and fitness for treatment.
- Further research is required to determine if age, in itself, is a determinant of curative prostate cancer treatment.

Prostate cancer

The prostate is a small gland about the size of a walnut that surrounds part of the urethra, which carries urine from the bladder to the penis. Prostate cancer can develop when the cells of the prostate grow in an uncontrolled way. Most tumours are slow-growing and may never cause symptoms. However, sometimes the disease is more fast-growing and aggressive and requires treatment to prevent it spreading.

Often, prostate cancer is picked up by biopsy after a Prostate Specific Antigen test (PSA), which detects elevated levels of a protein released by the prostate into the blood. The higher the level of PSA, the greater the likelihood of cancer being present. However, benign prostate conditions can also result in elevated PSA and only a proportion of men who have a raised PSA result are likely to have prostate cancer. It is therefore not recommended as a screening test for prostate cancer (Burford, Kirby et al., 2009).

Figure 1: World age-standardised incidence and mortality rates for prostate cancer
Source: International Agency for Research on Cancer (Globocan), 2008



Between 1994 and 2005, age-adjusted incidence of prostate cancer in RoI rose by 7% per annum, the largest increase in any of the common cancers (Donnelly, Gavin et al., 2009). In both NI and RoI, rates are rising faster in younger than older men (Carsin, Drummond et al., 2010). Over the past two decades, significant increases in incidence have also been reported in other countries due to increased PSA testing. Variation in testing has led to international differences in the incidence of prostate cancer, as shown in Figure 1.

The latest figures show that prostate cancer is an important cause of death in Ireland. In 2010 it was responsible for 245 deaths in Northern Ireland (NISRA, 2011) and 521 in RoI (CSO, 2011). More detailed figures show that deaths occur predominantly among older men – see Table 1.

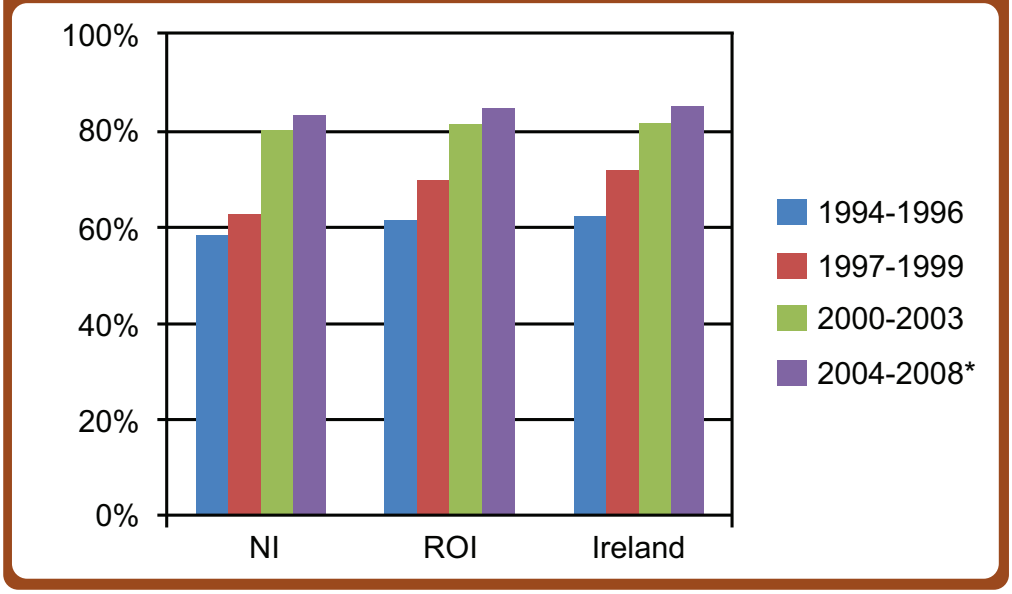
Table 1: Prostate cancer deaths by age-group, 2010

Age range	35-44	45-54	55-64	65-74	75-84	85+
ROI	1	2	38	101	200	179
NI	0	2	25	57	97	64

Survival rates

Despite rising incidence, the death rate for people with prostate cancer is falling. Marked improvements have occurred in survival rates in Ireland five years after diagnosis of prostate cancer. Figure 2 shows that survival rates in NI improved slightly more than in RoI, with the result that they were almost equal in the period 2004-2008. In Ireland as a whole, 5-year survival rates increased from slightly over 60% to more than 80% over the period covered. Not all the improvement is due to better treatments. Another significant factor is that increased PSA testing identifies many less serious diseases, especially among younger men, and does so at an earlier stage (when longer survival periods could be expected).

Figure 2: 5-year relative survival from prostate cancer for 1994-1996 to 2004-2008 Source: Donnelly et al., 2012)



Five-year survival rates in 2004-2008 were higher in RoI than in NI for all men under the age of 75 but this was reversed for men aged 75-99. In both parts of Ireland, men aged 45-54 had the highest survival rates, above 90% five years after diagnosis of prostate cancer, followed by men aged 18-44 (about 90%) and 55-64 (about 85-90%). After that there was a substantial decline to just over 70% for men in the 65-74 range and around 50% for the oldest men.

Treatment

Various guidelines on the investigation and treatment of prostate cancer have been issued in the UK, Europe and USA but evidence is unclear as to the best treatment. Several treatment options are available including curative radiotherapy, radical prostatectomy (removal of the prostate gland) or adjuvant chemical androgen deprivation therapy, which suppresses the male hormones to stop, slow down or reverse the growth of cancerous tissue. These treatments are associated with risk of psychological, psychosocial and physical side-effects of, including urinary or bowel incontinence and sexual dysfunction, poorer quality of life and distress.

According to Donnelly et al. (2012), the general lack of certainty that exists in prostate cancer treatment also applies to older men. Moreover, understanding of best practice in the treatment of older men is hindered by an under-representation of over 65s in cancer treatment trials (Hutchins, Unger et al., 1999). Many of the guidelines are formed on the basis of studies that excluded patients based on older age, poor performance status and a perception that that older patients are not suitable candidates for more aggressive therapy (Townsley, Selby et al., 2005).

Curative treatment has been reported to result in significantly improved life-expectancy and quality adjusted life-expectancy for older men presenting with few co-morbidities and moderately/poorly differentiated localised prostate cancer (Alibhai, Naglie et al., 2003). A study of treatment and survival in men aged 65-80 suggested that a survival advantage is associated with active treatment for low and intermediate-risk prostate cancer (Wong, Mitra et al., 2006). In contrast, aggressive treatment in men aged 75-84 was associated with significant decreases in disease-specific health related quality of life, with minimal reduction in absolute risk of dying from prostate cancer (Hoffman, Barry et al., 2006). Other studies found that carefully selected older patients, even those in their 80s, may benefit from radical prostatectomy or radiotherapy.

Trends identified by CARDI funded study

Diagnosis & Incidence

Against this background of uncertainty, the research team studied data in the cancer registries in RoI and NI, on treatment for prostate cancer for men aged 70 or more years and under 70 years. A combined database, covering more than a decade, showed 7,481 men who had been diagnosed with prostate cancer, 1,888 in NI and 5,593 in RoI.

In the years 2004-08 the incidence rate of prostate cancer for older men (70+ years) was almost 12 times higher than for younger men (782 cases per 100,000 compared with 68). Mortality rates from prostate cancer were 74 times higher for men aged 70+ (318 per 100,000) than for men under 70 (4.3 per 100,000).

Prostate cancer incidence (new cases diagnosed) was higher in RoI than in NI for both age groups. Death rates were similar in both parts of the country for the younger men but were higher in RoI for men aged 70+.

In RoI incidence rates among younger men (less than 70 years) rose by 15% per year between 1996 and 2004 and then levelled off. In NI an annual rise of 10% continued from 1994 to 2008. Among the older men, there was no change in incidence in NI; in RoI the rate increased by 4% between 1994 and 2002 but then declined by 2% annually. Mortality trends were similar north and south. Among men under the age of 70, mortality declined by 2% per year and for older men by 1% per year.

An unusual pattern emerges when patients are divided into five quintiles according to the socio-economic status of the areas where they live. In NI the lowest rates of prostate cancer are found among people living in the least deprived areas (1% below average) and the most deprived areas (4% below average). RoI is a mirror image because people in the least deprived areas are 5% more likely to have the disease and people in the most deprived areas are 7% more likely. However, Donnelly et al. (2012) say there may not be a genuine socio-economic deprivation difference since the results could be an artefact of how deprived areas are defined or could reflect differences in the two systems or the profile of men taking PSA tests.

Treatment received

Table 2 shows the numbers of older and younger men in NI and RoI who saw a urologist and received one of the main forms of treatment.

Table 2: Percentage of prostate cancer patients by treatment (Source: Donnelly et al., 2012, total database)

	Northern Ireland		Republic of Ireland	
Age	Under 70	70+	Under 70	70+
Seen by urologist	79%	62%	88%	69%
Radical prostatectomy	14%	<1%	25%	1%
Radical radiotherapy	18%	7%	19%	5%
Adjuvant hormone therapy with radiotherapy	8%	3%	5%	1%

Hormone therapy is excluded due to concerns about the completeness of the data. Also it is often regarded as the default non-curative treatment and the focus of the study was curative treatment. Chemotherapy is excluded because it is rare and is considered a palliative treatment.

In the decade 1996-2006 men aged 70+ were 22% less likely to see a urologist (67%) than younger men (86%) in Ireland as a whole. Over the ten years the proportion of men who saw a urologist in NI increased sharply from 59% to 94%; this put it ahead of RoI where the proportion remained stable at 81%.

In 2006, men living in the most deprived areas (78.5%) were less likely to see a urologist than men from the least deprived areas (90.6%). Unmarried men were 17% less likely to see a urologist than those who are married and rural men were 12% less likely to see the specialist than urban dwellers. Men in RoI were much more likely than those in NI to be treated in private hospitals. These privately treated patients were more likely to see a urologist than men treated in public hospitals only.

In all three periods studied, 11% of men had a radical prostatectomy but 96% of the 802 operations (769) were performed on men under the age of 70 and only 33 on older men. Looking at proportions, in 2006, 25.7% of younger men and 0.9% of older men had the operation. Men in RoI were much more likely to have a radical prostatectomy (17%) than those in NI (7%) in 2006; married men were almost three times more likely to have it than single men (20% compared with 7%, adjusted for age); and men from the least deprived areas were 77% (or 1.77 times) more likely to have it (19.5%) than men in the most deprived areas (8.5%).

The proportion of younger men (<70 years) receiving radical radiotherapy more than doubled in the ten year period to 22.3% in 2006; the increase among older men was slower and reached 10% at the end of the period. Over the entire period, younger men were three times more likely to have this treatment than older men. Importantly, however, after adjusting for a range of patient and clinical factors, men aged 70+ are 72% less likely to receive radical radiotherapy than younger men. Only small differences were observed between NI and RoI but married men were more likely to have radical radiotherapy than men living alone and people in private hospitals were more likely than those in public ones. In NI men living in the most deprived areas had less chance of receiving the treatment but this social gradient did not exist in RoI.

Over the entire period, 5% of men in NI and 3% in RoI received adjuvant hormone and radiotherapy; again younger men were more likely (5%) than older men (2%) to receive this treatment. There were no differences by urban/rural or levels of deprivation in the likelihood of patients receiving adjuvant hormone and radiotherapy. Finally, statistics on transurethral resection of the prostate (TURP) are available only for NI. Older men are more likely to have this treatment (27%) than men under 70 (18%) but TURP is becoming less common, being used on 49% of men in 1996 and only 11% in 2006.

Survival analysis

The research team carried out a statistical analysis to estimate the ‘hazard ratio’ of dying from prostate cancer within two years – i.e. the chance of dying in one category compared with another. The variables considered are listed in Table 3 and the hazard ratios for these variables are estimated taking into account the other variables. Some way to interpret the table is that, for example, people aged 70+ had a 1.93 times higher risk of dying

than people less than 70 years (i.e. nearly double the risk). Taking another example, people in RoI are more than twice as likely (2.24 times greater) to die from prostate cancer within two years as men in NI. However, this is due largely to the higher proportion of Stage IV patients in NI relative to ROI. Further study is needed to assess the comparability of stage data between the two countries.

Table 3: Relative risk of death comparing different levels of explanatory variables (Source: Donnelly et al., 2012)

Effects	Hazard Ratio	P-value
Age 70+ vs age<70	1.93	<.001
RoI vs NI	2.24	<.001
Year 2006 vs year 1996	0.57	<.001
Year 2001 vs year 1996	0.78	<.001
Private vs public Hospital	0.78	0.04
Married vs unmarried	0.86	0.01
Stage IV vs stage I & II	6.20	<.001
Stage III vs stage I & II	1.78	<.001
Grade 3 & 4 vs grade 1	2.17	<.001
Radical prostatectomy and radical radiotherapy vs no radical treatment	0.23	<.001
Seen by urologist vs not seen	0.48	<.001

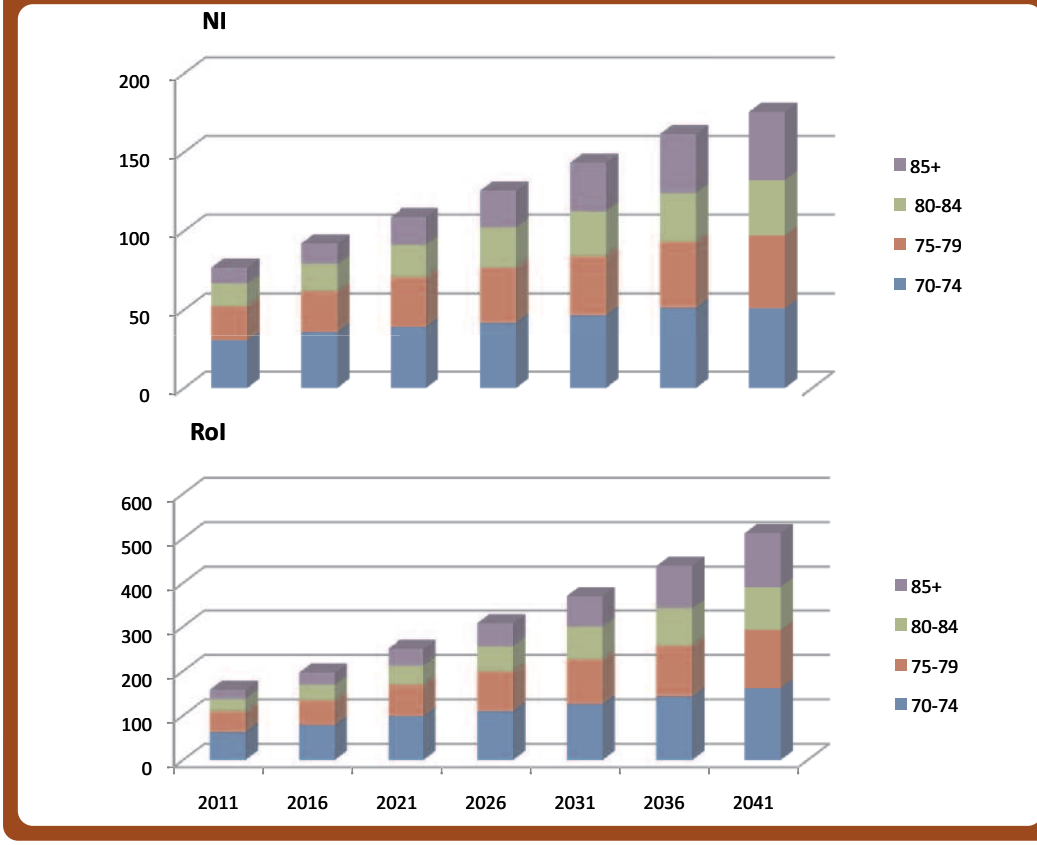
To summarise Table 3, the factors associated with better survival were being younger, more recently diagnosed, attending a private hospital, being diagnosed with early stage disease, being seen by a urologist and having a radical prostatectomy.

Policy implications

> *"With increasing life expectancy the importance of prostate cancer investigation and treatment will increase. It is therefore important to document treatment patterns, mortality and survival in older men on the Island of Ireland" (Donnelly et al., 2012: 49).*

The ageing impact can be seen in Figure 3, which shows that the number of men aged 70 and over is projected almost to triple in Ireland as a whole over the next 30 years. Numbers will rise by an expected 100,000 in NI (130%) and by 350,000 (220%) in RoI.

Figure 3: Projected number of men in Ireland aged 70 and over, 2011-2041 (thousands)
Source: CARDI, using data from CSO and NISRA



Age and life expectancy

The study confirmed the initial hypothesis that there are substantial differences in the extent to which older and younger men are seen by urologists and in the likelihood of older men receiving radical treatment compared with younger men. However, the researchers recognise that the differences may not result from age in itself but from other clinical factors. They suggest the need for a shift in focus from age to life expectancy[1].

In this study, no information was available on patients' life expectancy. Although data existed on co-morbidity in NI, this only provided information on the presence or absence of co-morbidity with no information on severity. In addition, there was no information available on dependence status or nutritional status.

> *Thus, we cannot, with confidence, attribute the entire observed differences in the likelihood of men receiving care to their age alone: these other factors are also likely to be important. In summary, it is not possible to measure under-treatment in older men without accounting for older men who should not have curative treatment due to having low life-expectancy (Donnelly et al, 2012: 51).*

1 Guidelines from the International Society of Geriatric Oncology (SIOG) on the treatment of elderly men (Droz et al., 2010) propose that a patient's life-expectancy, and not age, should determine clinical decision-making as life-expectancy will determine if a patient is likely to experience a survival benefit from treatment. The SIOG guidelines identify a method to assess life-expectancy using co-morbidity, dependence status and nutritional status.

Other factors

Incidence of prostate cancer among socio-economic groups differed between RoI and NI. In RoI, both the most affluent and most deprived were the most likely to be diagnosed with prostate cancer. A possible explanation is that in RoI, 32% of the population on low incomes or unemployed receive free health care through the medical card system, and secondly, many people from affluent areas will have private health insurance. In NI, where the vast majority of men receive their health-care through the National Health Service, distribution across the socio-economic levels was more uniform.

In RoI, there was a declining gradient in the percentage of men seen by a urologist with increasing socio-economic deprivation; this was not observed in NI. Since nearly one-third of people in RoI get free medical care, this difference may be less about ability to pay than about the organisation and accessibility of services and being less likely to attend urologists' appointments.

Implications for further research

- The research team proposes a survey of clinicians' use of guidelines, particularly on using life expectancy in treatment decisions. An assessment of a patient's life expectancy should be recorded in the medical chart at the time of diagnosis.
- Research is needed on the factors which are likely to impact on decision processes in the treatment of prostate cancer e.g. information gathered at multidisciplinary team meetings, or studies involving clinicians and other healthcare professionals.
- To understand the extent to which patients' attitudes affect treatment patterns, research is needed to compare older and younger patients' experiences of diagnosis and treatment decision-making.
- Further clinical trials are needed specifically on treatment of older men for prostate cancer to better underpin future clinical guidelines for this growing patient group.

Conclusion

The incidence of prostate cancer is rising and it remains a significant cause of death on the island of Ireland (although this is decreasing). It is also receiving a good deal more attention from researchers, politicians and the media, especially in RoI. For example, a recent report by Professor Ciaran O'Neill and Dr Mary Stiles, NUI Galway (2011), found that having private medical insurance was the main factor explaining differences in the uptake of services for breast, prostate, colorectal and cervical cancer.

This CARDI funded study confirmed significant differences in the diagnosis and treatment of men aged 70 and older compared with younger men in both RoI and NI. This has important implications for policy makers and practitioners in the health services, as well as for researchers seeking to identify the causes of these differences.

The report also finds that a balance must be struck between giving aggressive treatment and ensuring that the men involved have as good a quality of life as possible. Diagnosis and treatment may extend life and will often be the preferred option but they may also have harmful side effects which can reduce quality of life.

Published by the Centre for Ageing Research and Development in Ireland (CARDI) ©. CARDI has produced this publication as a resource for researchers, policy-makers, older people and others with an interest in ageing research. To find out more about CARDI's grants programme please visit www.cardi.ie

This research brief is based on findings from a research project funded under CARDI's Grants Programme: Donnelly et al (2012) and information collated by CARDI.

It may be cited as Is age a determining factor in the treatment of men with prostate cancer? Dublin: Centre for Ageing Research and Development in Ireland, 2012.

This publication can be downloaded from **www.cardi.ie** Additional copies may be requested from:

Centre for Ageing Research and Development in Ireland
Forestview, Purdy's Lane,
Belfast BT87ZX
Tel: +44 (0) 28 9069 0066

Centre for Ageing Research and Development in Ireland
5th Floor Bishop's Square,
Redmond's Hill, Dublin 2
Tel: +353 (0) 1 478 6308

Email: **info@cardi.ie**

Our work has been made possible through funding by The Atlantic Philanthropies, augmented by grants from the Department of Health and Children in Dublin and the Health and Social Care Research Office, Public Health Agency, Northern Ireland. CARDI is hosted by the Institute of Public Health in Ireland.

Research Team

Dr Anna Gavin
Northern Ireland Cancer Registry

Dr Linda Sharp
National Cancer Registry Ireland

Mr Conan Donnelly
Queen's University Belfast

Dr Finian Bannon
Northern Ireland Cancer Registry

Dr Sandra Deady
National Cancer Registry of Ireland

References

Alibhai SM, Naglie G, Nam R, Trachtenberg J, Krahn MD (2003). *Do older men benefit from curative therapy of localized prostate cancer?* J Clin Oncol 21:3318–27.

Burford D, Kirby M, Austoker J (2009). *Prostate cancer risk management programme, information for primary carers. PSA testing in asymptomatic men*, NHS.

Carsin A, Drummond FJ, Black A (2010). *Impact of PSA testing and prostatic biopsy on cancer incidence and mortality: comparative study between the Republic of Ireland and Northern Ireland*. Cancer Causes Control 21: 1523-31.

Central Statistics Office (2011). *Vital statistics: Fourth Quarter and Annual Summary 2010*, available at http://www.cso.ie/releasespublications/documents/vitalstats/2010/vstats_q42010.pdf

Department of Health, Social Services and Public Safety (2007). *Regional Cancer Framework: A Cancer Control Programme for Northern Ireland*. DHSSPS.

Donnelly DW, Gavin AT and Comber H (2009). *Cancer in Ireland 1994-2004: A comprehensive report*. NI Cancer Registry and National Cancer Registry Ireland.

Donnelly, Conan; Bannon, Finian; Sharp, Linda; Deady, Sandra; and Gavin, Anna (2012). *Is age a determining factor in the treatment of men with prostate cancer?* Belfast: Northern Ireland Cancer Registry.

Droz JP, Balducci L, Bolla M, Emberton M, Fitzpatrick JM, Joniau S, Kattan MW, Monfardini S, Moul JW, Naeim A, van Poppel H, Saad F, Sternberg CN (2010). *Management of prostate cancer in older men: recommendations of a working group of the International Society of Geriatric Oncology*. BJU Int. 2010a Aug;106(4): 462-9.

Hoffman RM, Barry MJ, Stanford JL, Hamilton AS, Hunt WC, Collins MM (2006). *Health outcomes in older men with localized prostate cancer: results from the Prostate Cancer Outcomes Study*. Am J Med 119(5): 418-25.

Hutchins LF, Unger JM, Crowley JJ, Coltman Jr CA, Albain KS (1999). *Underrepresentation of patients 65 years of age or older in cancer treatment trials*. N Engl J Med341: 2061–7.

Northern Ireland Statistics & Research Agency (2011). *Statistical Bulletin: Deaths in Northern Ireland (2010)*, available at http://www.nisra.gov.uk/archive/demography/publications/births_deaths/deaths_2010.pdf

Townsley CA, Selby R, Siu LL (2005). *Systematic review of barriers to the recruitment of older patients with cancer onto clinical trials*. J Clin Oncol 23: 3112–24.

Wong YN, Mitra N, Hudes G, Localio R, Schwartz JS, Wan F, Montagnet C, Armstrong K (2006). *Survival associated with treatment vs observation of localized prostate cancer in elderly men*. JAMA 296(22): 2683-93.