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Penile Cancer Report: Malignant and In-Situ Tumours

Urology SSCRG

THE BRITISH ASSOCIATION OF UROLOGICAL SURGEONS

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Contents

1. Report Background

This report examines trends in incidence, mortality and survival of penile cancers, both malignant and penile epithelial neoplasia (PIN) (ICD10 C60 & D074) in England over the most recent 20 years of data available 1990-2009. This report also endeavours to examine treatment pathways for penile cancer including modality of treatment, an analysis of penile specific surgeries, amputation, partial amputation and reconstruction, time between curative surgery and reconstruction, whether a patient receives reconstruction and whether this is influenced by the patients' relative level of socio-economic deprivation.

Data used in this report has been sourced from:

National Cancer Data Repository 2009 (NCDR)
British Association of Urological Surgeons Dataset (BAUS)
Hospital Episode Statistics (HES)

2. Methodology

All cases of penile cancer and penile epithelial neoplasia (ICD10 C60 & D074) diagnosed between 1990 and 2009 were extracted from the NCDR. Extra data on stage and grade were appending from the BAUS dataset. Treatment data, where available, were added from the HES dataset. This is primarily a source for surgical data. Analysis contained in this report was conducted on the composite database.

3. Penile Cancer Background

Penile cancer in England, and in other western counties, is a very uncommon disease. Typically a rate of just 1 case per 100,000 males is observed in Western Europe and North America (Pizzacaro 2009).

In the developing world, particularly sub-Saharan African countries the rate is significantly higher. In Uganda, for example, a rate of 10 per 100,000 males is observed (Pizzacaro 2009).

There has been less formal guidance on management of penile tumours in the UK, compared to other urological cancers (e.g Improving Outcomes in Urological Cancers guidance). This is possibly due to its rarity.

There are several histological types of penile cancer. The vast majority of penile cancers diagnosed are squamous cell carcinomas, in excess of 90%.

- Squamous cell carcinomas: Skin like cells, grow on surface of the penis. Generally slow growing. They are curable if discovered early.
- Adenocarcinoms: Account for approximately 5% of penile cancers. Develop in the glandular cells.
- Basal cell Carcinomas: Develop from basal cells (found at the base of the skin structure). Account for approximately 2% of all penile cancers.
- Melanoma: As with basal cell carcinomas, melanomas are comparatively rare, accounting for 2% of penile cancers. Arise from melanocytes, the cells which give the skin colour.
- Sarcomas: Sarcomas are tumours which arise in the connective tissue. These are generally faster growing tumours but are rare, accounting for around 1% of penile cancer.

Tumours can develop anywhere on the penis, but the most common sites are the foreskin and glans.

Cancers that have not invaded beyond the level of the epithelium of the penis are known as carcinoma in situ (CIS) or sometimes penile intraepithelial neoplasia (PIN) (ICD10 D074). This is similar to cervical intraepithelial neoplasia (CIN) and anal intraepithelial neoplasia (AIN).

Tumours that have extended beyond the superficial skin level into connective tissue below the skin or into deeper layers are classified as malignant tumours (ICD10 C60).

Variation in penile cancer incidence is observed between different racial/ethnic groups, religio-cultural practices, particularly circumcision.

Risk Factors:

- Human Papilloma Virus (HPV): Several studies have shown HPV infection to increase the risk of penile cancer (as well as several other cancers) (Pow-Sang 2010). HPV is a sexually transmitted disease and around 80% of the UK population will become infected at some point in their lives. Around half of all men diagnosed with penile cancer, also have evidence of infection with a variant of HPV.

- A weak or depressed immune system: Men with AIDS or otherwise weakened immune systems are at an increased risk of penile cancer (ACS 2013).

- Poor personal hygiene (Minhas 2010).

- Phimosis: A condition where the foreskin cannot be fully retracted. It is hypothesised that phimosis can lead to a build up of smegma around and under the foreskin, which in itself is not thought to be carcinogenic, but rather increases the likelihood of infection and irritation (Pow-Sang 2010).

- Treatment of Psoriasis: A particular type of therapy for this skin condition known as PUVA (a combination of drug and light therapy) (ACS 2013).

- Genetic factors: A first line male relative with the squamous cell type of penile cancer increases risk by a factor of 8.

- As with many other cancers, tobacco, however imbibed, is a risk factor (Pow-Sang 2010).

Protective Factors:

- There is limited and mixed evidence on circumcision. Some papers suggest a protective factor for those circumcised at a young age (Larke 2011). However, the majority of US males are circumcised and the incidence of penile cancer is similar to the UK at 0.7 per 100,000 for 2006-10 (SEER statistics).

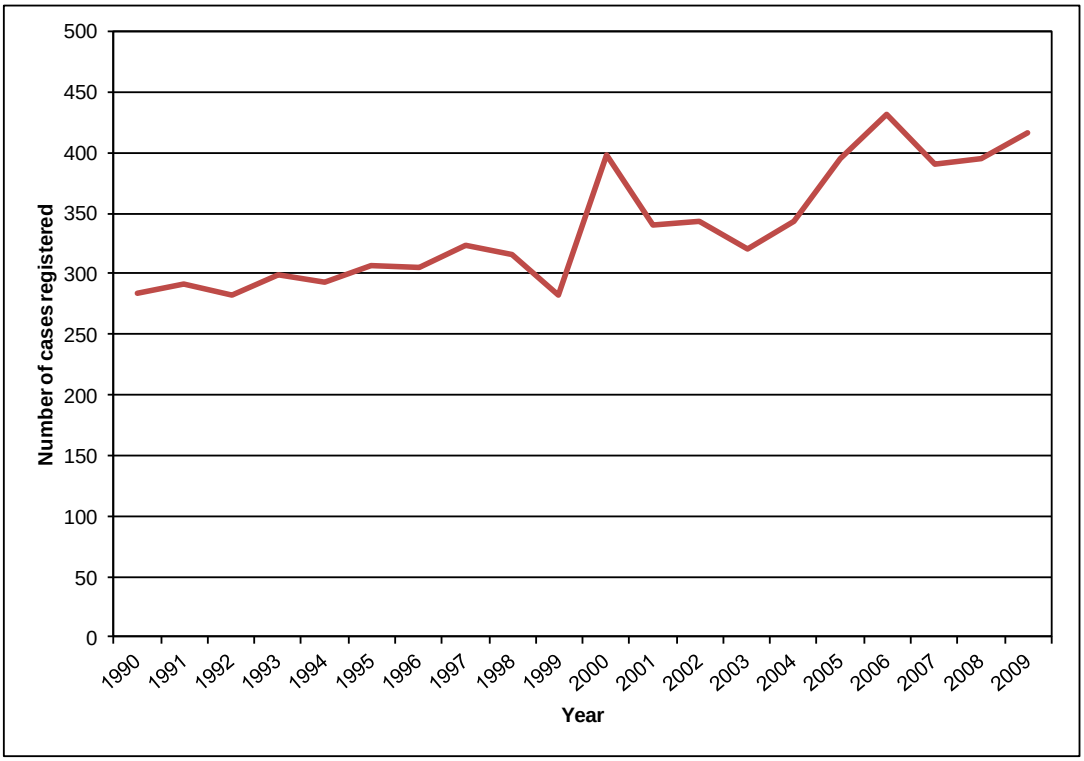
- Use of condoms: prevents the transmission of HPV (Bleeker 2009)

4. Incidence

4.1 Penile cancer (ICD10 C60)

There has been an increase in the number of diagnoses of penile cancer over the study period. In the period 1990-1992 859 cases of penile cancer were diagnosed (an average of 286 cases per year). This rises to 1,203 (an average of 401 cases per year) diagnosed between 2007 and 2009.

Figure 1: Number of cases of penile cancer in England, 1990-2009

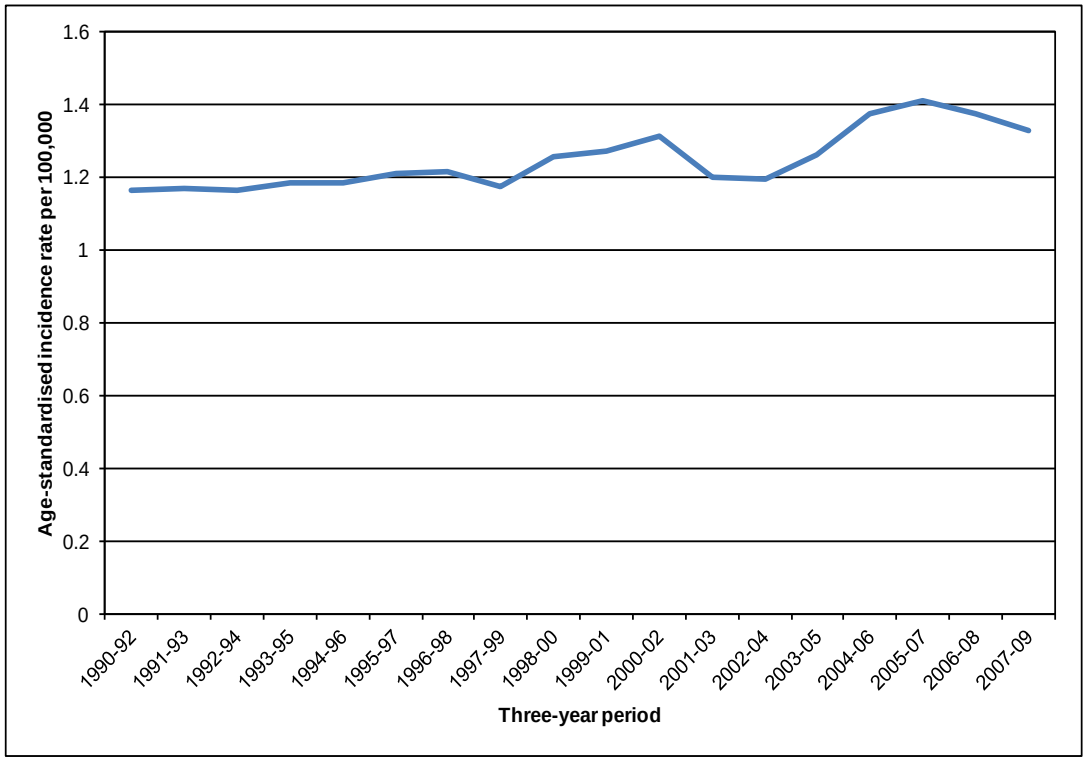


Source: National Cancer Data Repository; Office for National Statistics

Age standardised rates of penile cancer have increased over the last four three-year periods.

2004-06, 2005-07 and 2006-08 have significantly higher age standardised rates than their preceding non-overlapping three-year periods; 2001-03, 2002-04 and 2003-05 respectively ($p < 0.05$). The rate in the most recent three-year period of data, 2007-2009, (1.3 per 100,000) is not significantly higher than the preceding non-overlapping three-year 2004-2006.

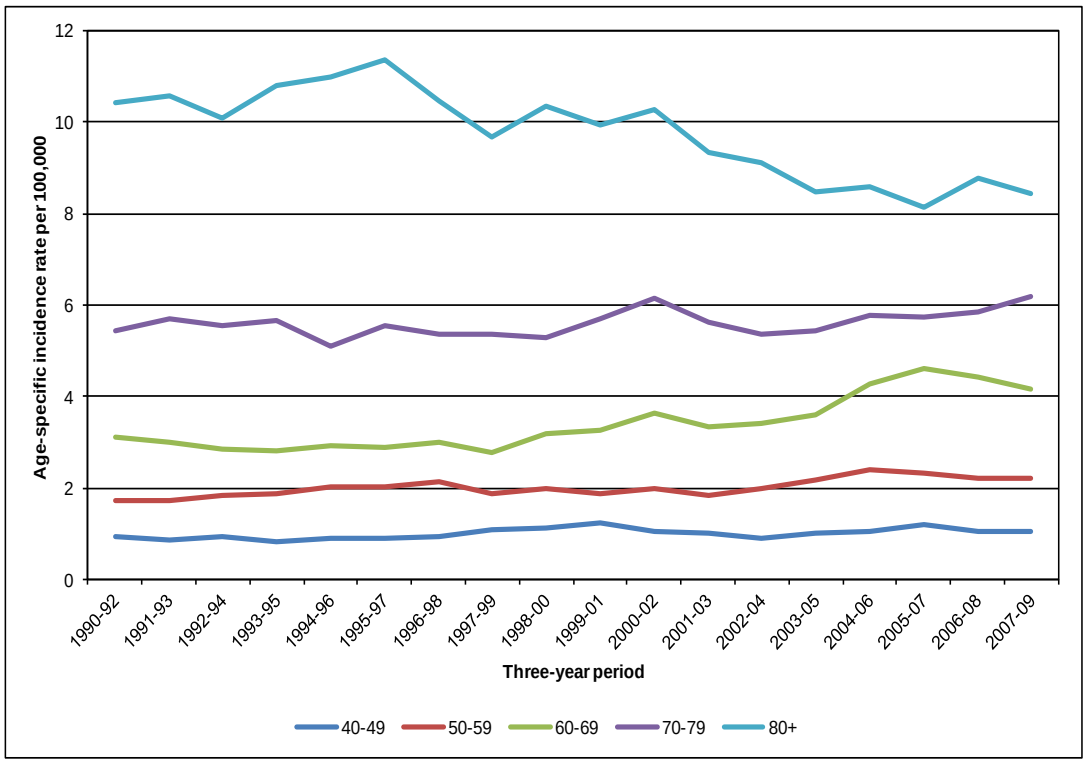
Figure 2: Incidence of penile cancer, age-standardised rate per 100,000, in England, 1990 – 2009



Source: National Cancer Data Repository; Office for National Statistics

Penile cancer is relatively rare in the younger age groups. There is an age specific rate of around 1 per 100,000 in the 40-49 age group and around 2 per 100,000 in the 50-59 age group. This rises to between 8 and 11 per 100,000 in the 80+ age group.

Figure 3: Incidence of penile cancer in males by age, rate per 100,000, in England, 1990-2009

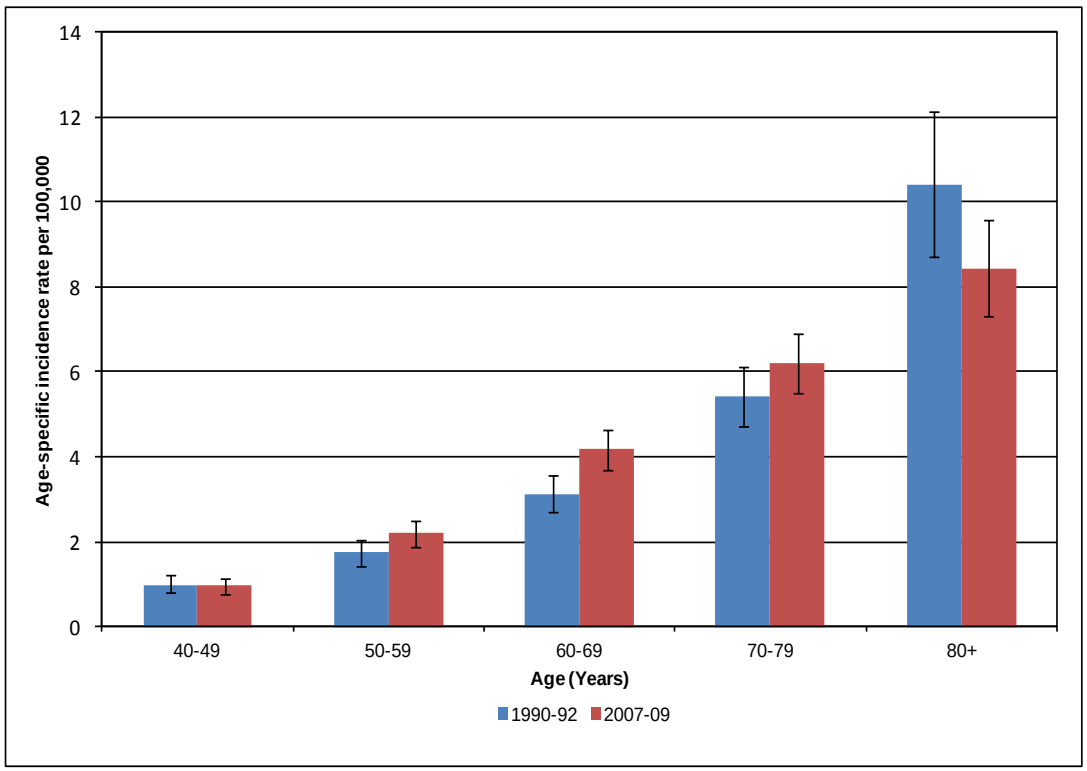


Source: National Cancer Data Repository; Office for National Statistics

Comparing age specific rates from the first three years (1990-92) to the last three years of the study (2007-09), the rates seen in the 50-59 and 60-69 age groups have increased significantly during this period (26% (p=0.03) and 33% (p=0.001) increase respectively).

No significant differences can be seen within the other age groups.

Figure 4: Age-specific incidence rates of penile cancer in males, rate per 100,000, in England, 1990-2009

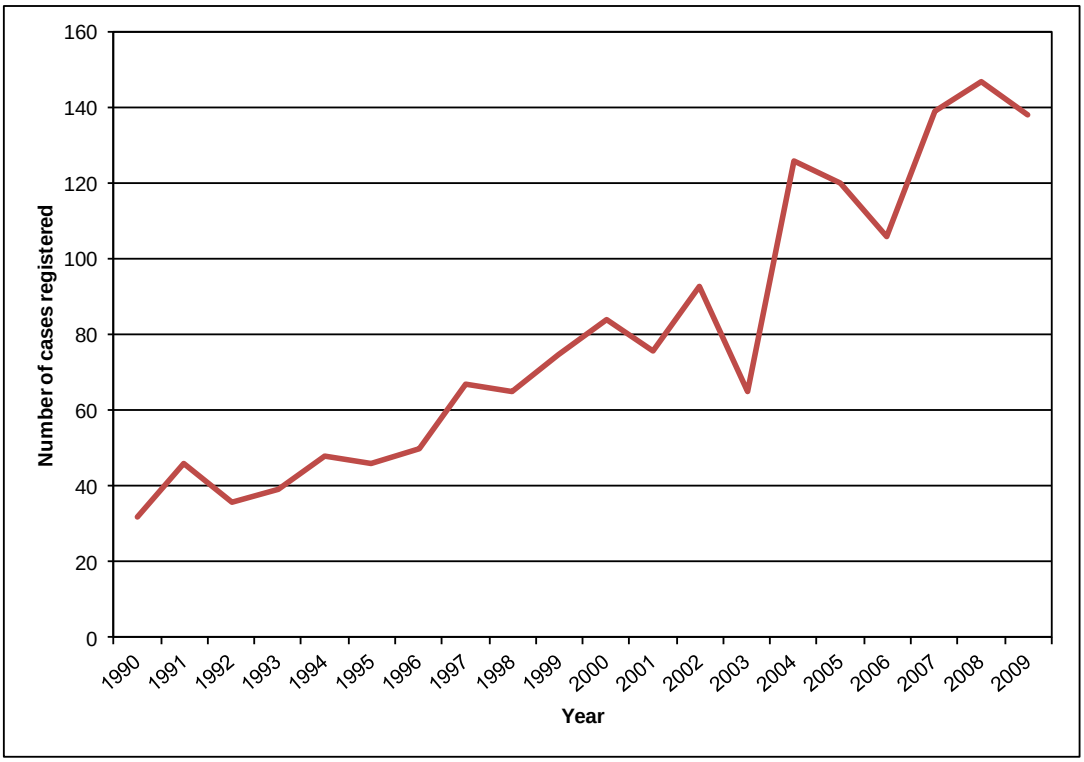


Source: National Cancer Data Repository; Office for National Statistics

4.2 Penile intraepithelial neoplasia (ICD10 D074)

There has been an increase in the number of diagnoses of PIN over the study period. In the period 1990-1992 114 cases of PIN were diagnosed (an average of 38 cases per year). This rises to 401 (an average of 141 cases per year) diagnosed between 2007 and 2009.

Figure 5: Number of cases of penile intraepithelial neoplasia in England, 1990-2009

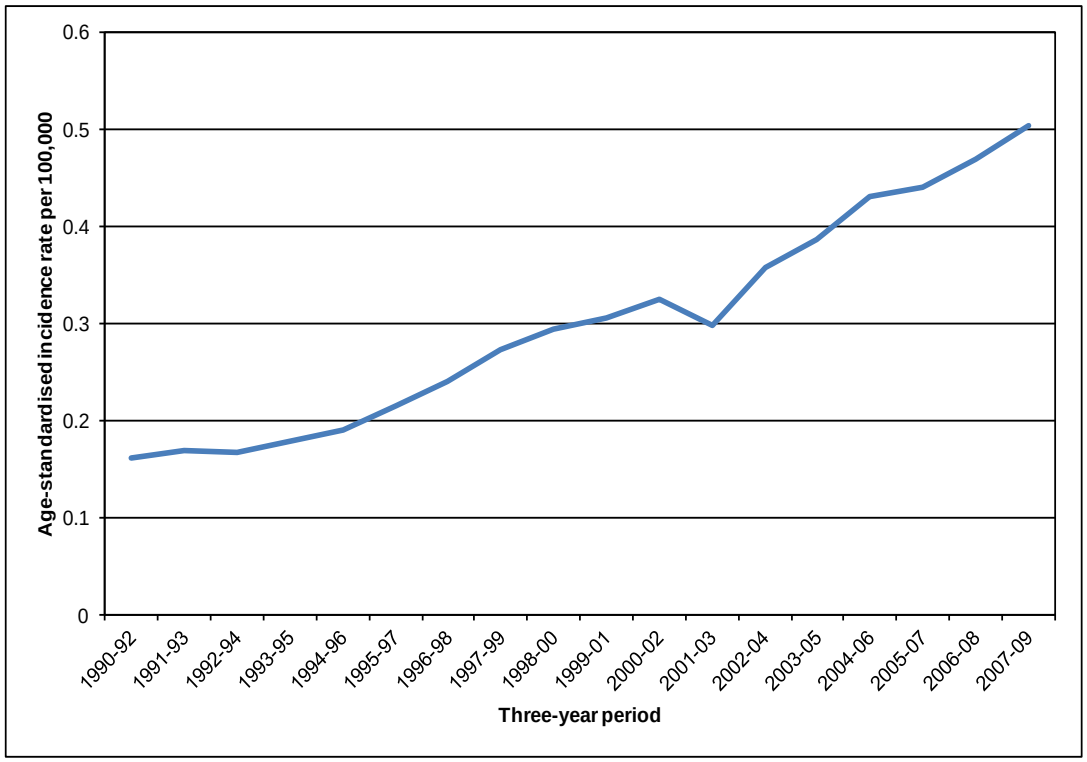


Source: National Cancer Data Repository; Office for National Statistics

Age standardised rates of PIN have increased over the last five three-year periods.

2004-06, 2005-07, 2006-08 and 2007-09 have significantly higher age standardised rates than their preceding non-overlapping three-year periods; 2001-03, 2002-04, 2003-05 and 2004-06 respectively ($p < 0.05$). The rate in the most recent three-year period of data, 2007-2009 is 0.5 per 100,000.

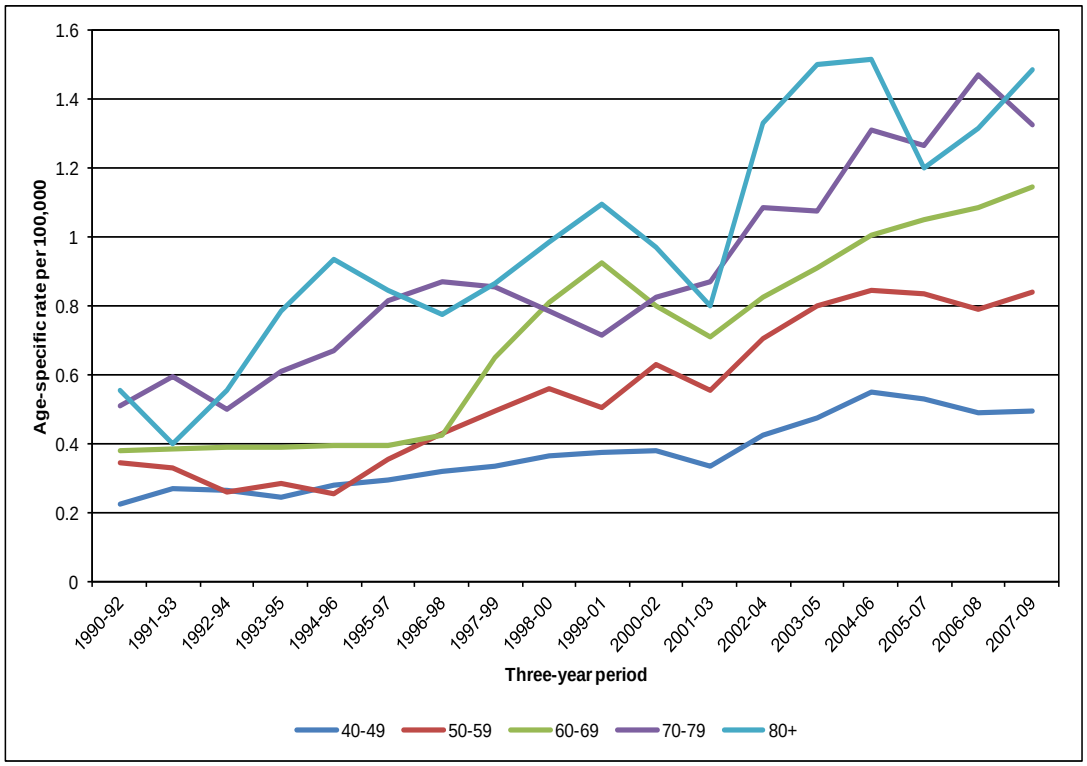
Figure 6: Incidence of penile intraepithelial neoplasia, age-standardised rate per 100,000, in England, 1990 – 2009



Source: National Cancer Data Repository; Office for National Statistics

PIN is comparatively rarer in the younger age groups. In the most recent three-year period, 2007-09, there is an age specific rate of around 0.5 per 100,000 in the 40-49 age group and around 0.8 per 100,000 in the 50-59 age group. This rises to 1.5 per 100,000 in the 80+ age group.

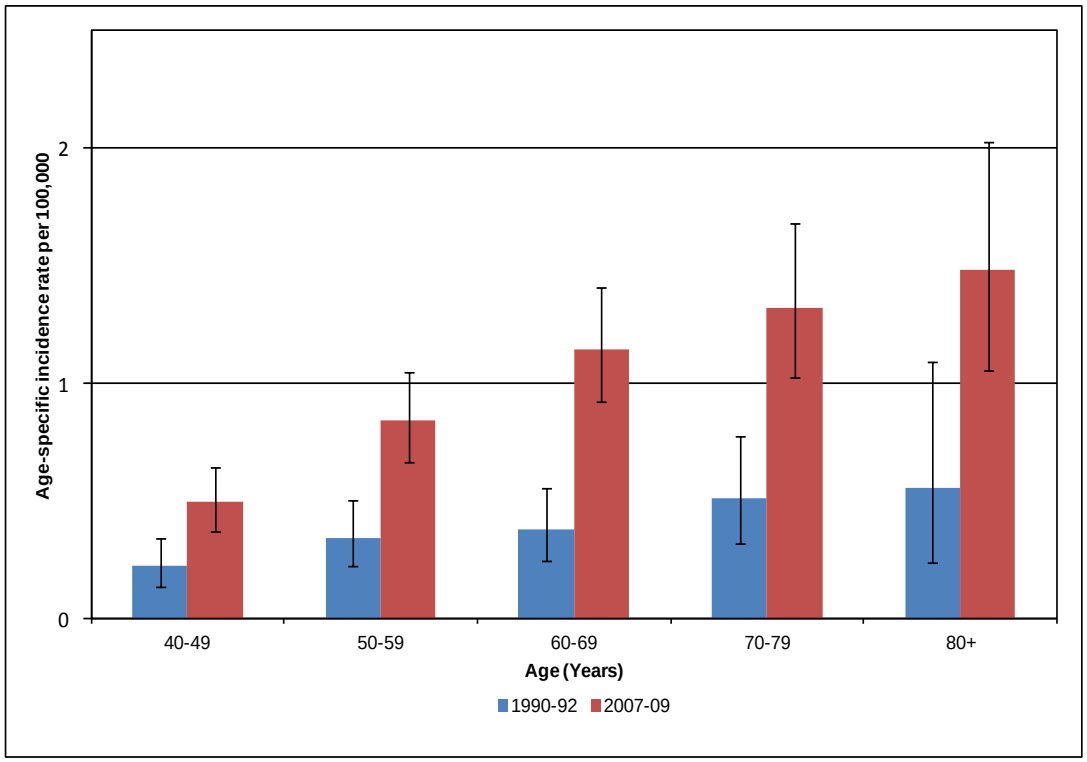
Figure 7: Incidence of penile intraepithelial neoplasia in males by age, rate per 100,000, in England, 1990-2009



Source: National Cancer Data Repository; Office for National Statistics

Comparing age specific rates from the first three years (1990-92) to the last three years of the study (2007-09), all age groups have increased significantly during this period ($p < 0.001$).

Figure 8: Age-specific incidence rates of penile intraepithelial neoplasia in males, rate per 100,000, in England, 1990-2009



Source: National Cancer Data Repository; Office for National Statistics

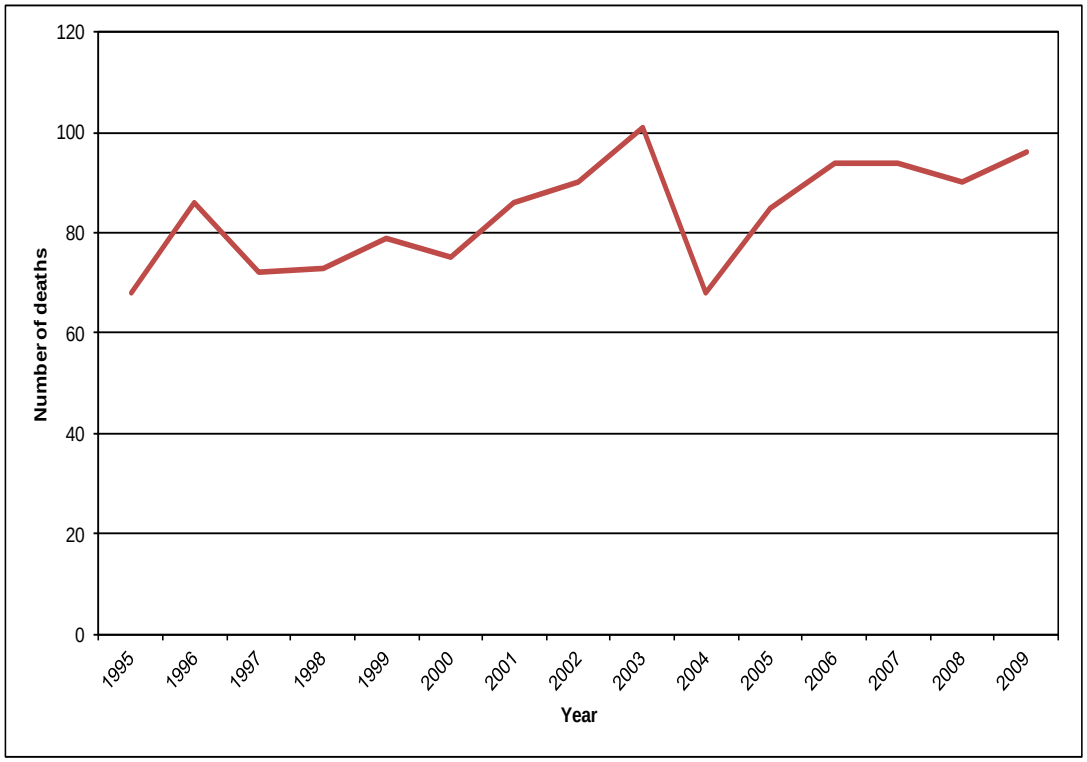
5. Mortality

5.1 Penile cancer (ICD10 C60)

Presentation of penile cancer is often delayed due to patient embarrassment, but treatment is effective if the lymph nodes are not involved or are removed and so mortality rates are low.

In all years except 2003, the number of people dying due to penile cancer is under 100.

Figure 9: Deaths from penile cancer in England, 1995-2009



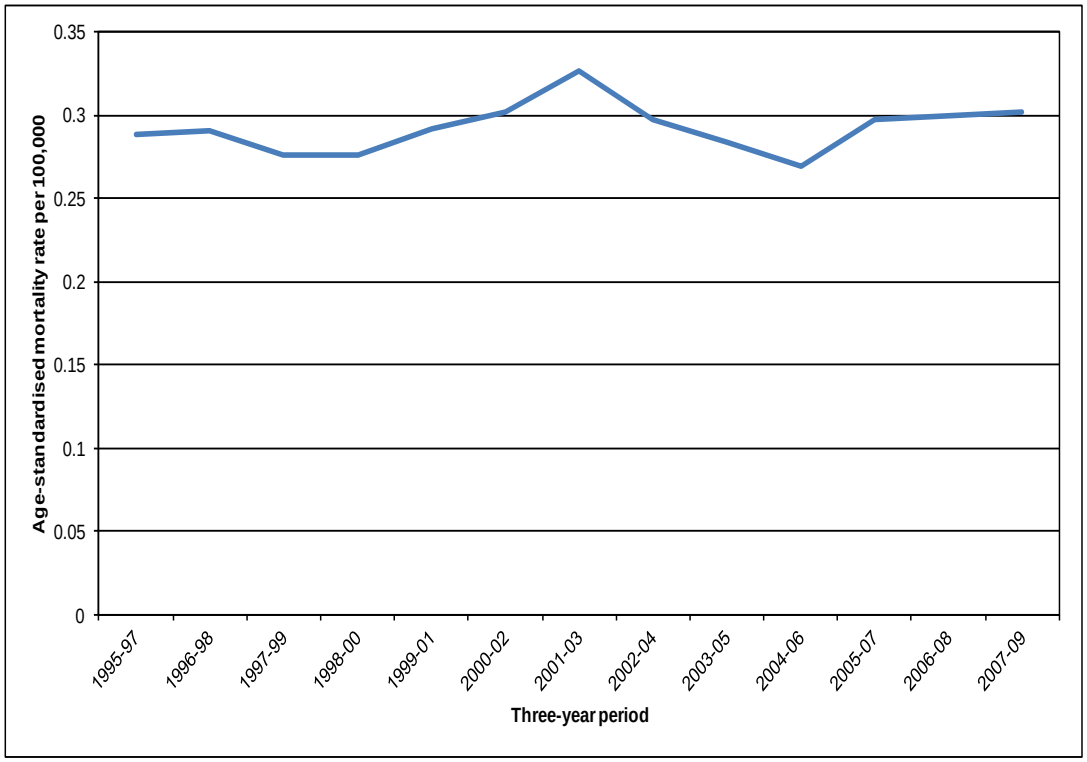
Source: Office for National Statistics

Age standardised mortality rates of penile cancer have remained relatively constant over the study period at 0.3-0.4 per 100,000.

The age standardised mortality rate in 2004-06 (0.27 per 100,000) is significantly lower than that seen in the previous non-overlapping three year period 2001-03 (0.33 per 100,000) ($p < 0.05$).

No significant differences can be seen between any of the other non-overlapping three year periods.

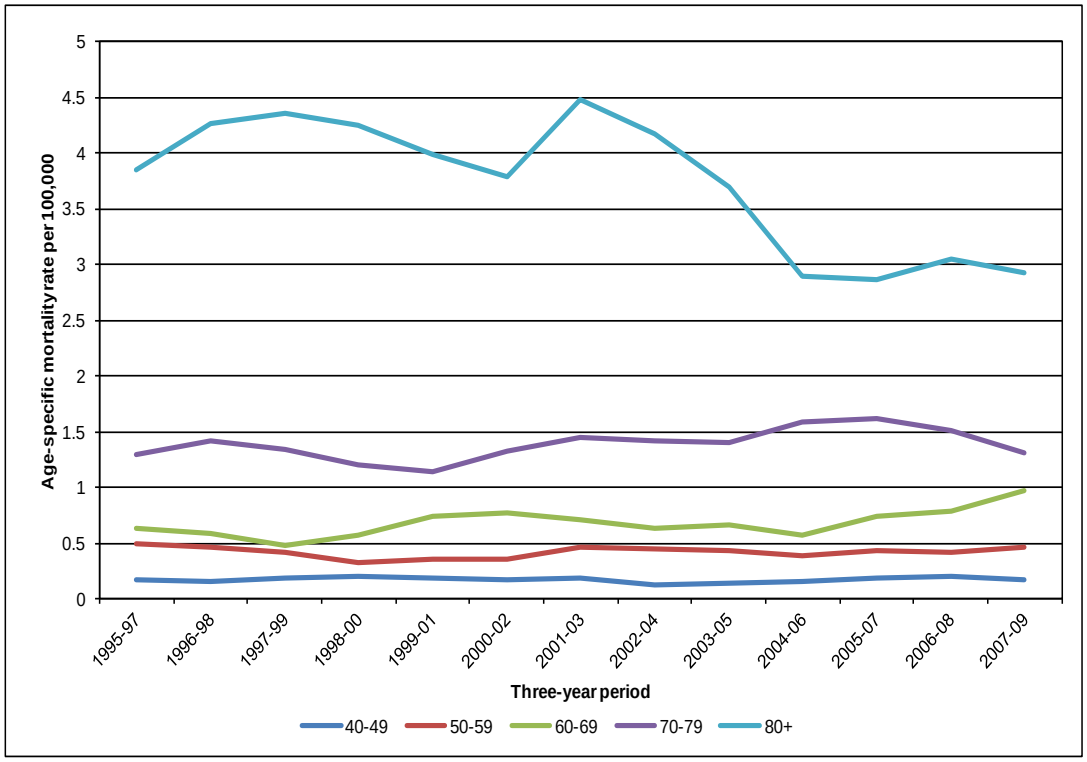
Figure 10: Mortality from penile cancer, age-standardised rate per 100,000, in England, 1995 - 2009



Source: Office for National Statistics

As with penile cancer incidence, mortality in the younger age groups is low, and has remained relatively constant in the 40-79 age groups. The age specific rate seen in the 80+ age group is higher than the other age groups but is more variable during the time period studied. The analysis of these rates is hampered by fluctuations induced by small numbers.

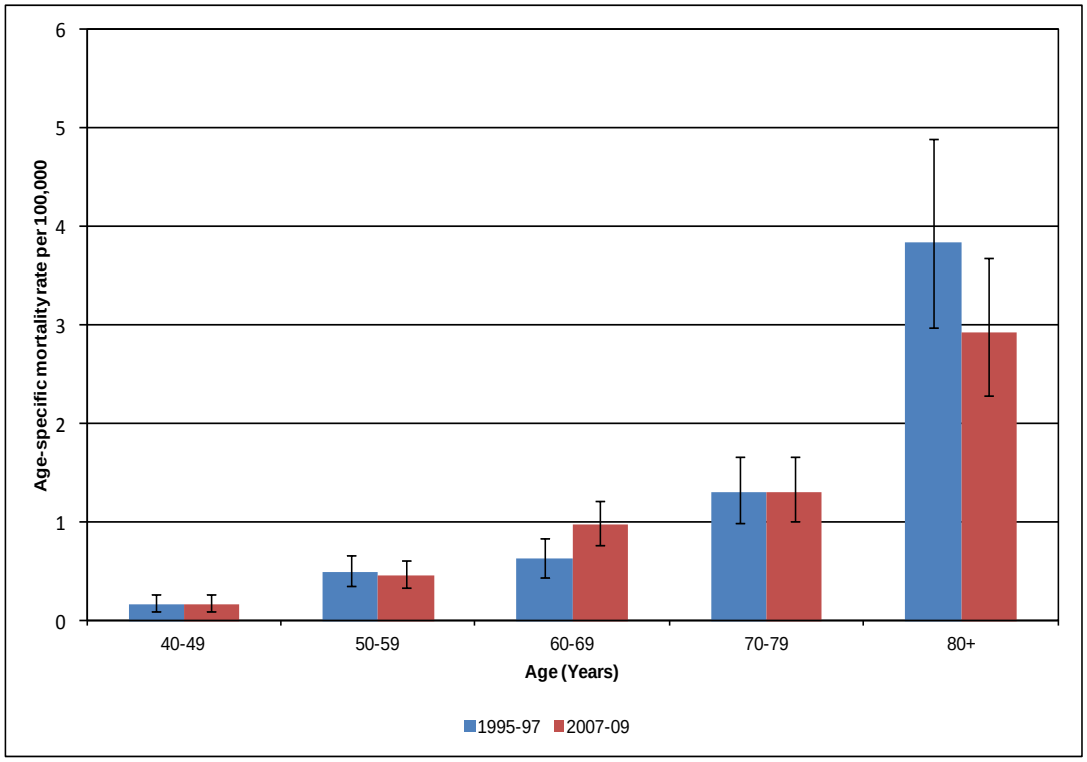
Figure 11: Mortality from penile cancer in males by age, rate per 100,000, in England, 1995-2009



Source: Office for National Statistics

The age specific mortality rate of penile cancer in men aged 60-69 increased between 1995-97 and 2007-09 by 56% (p= 0.02).

Figure 12: Age-specific mortality rates of penile cancer in males, rate per 100,000, in England, 1995-2009



Source: Office for National Statistics

5.2 Penile intraepithelial neoplasia (ICD10 D074)

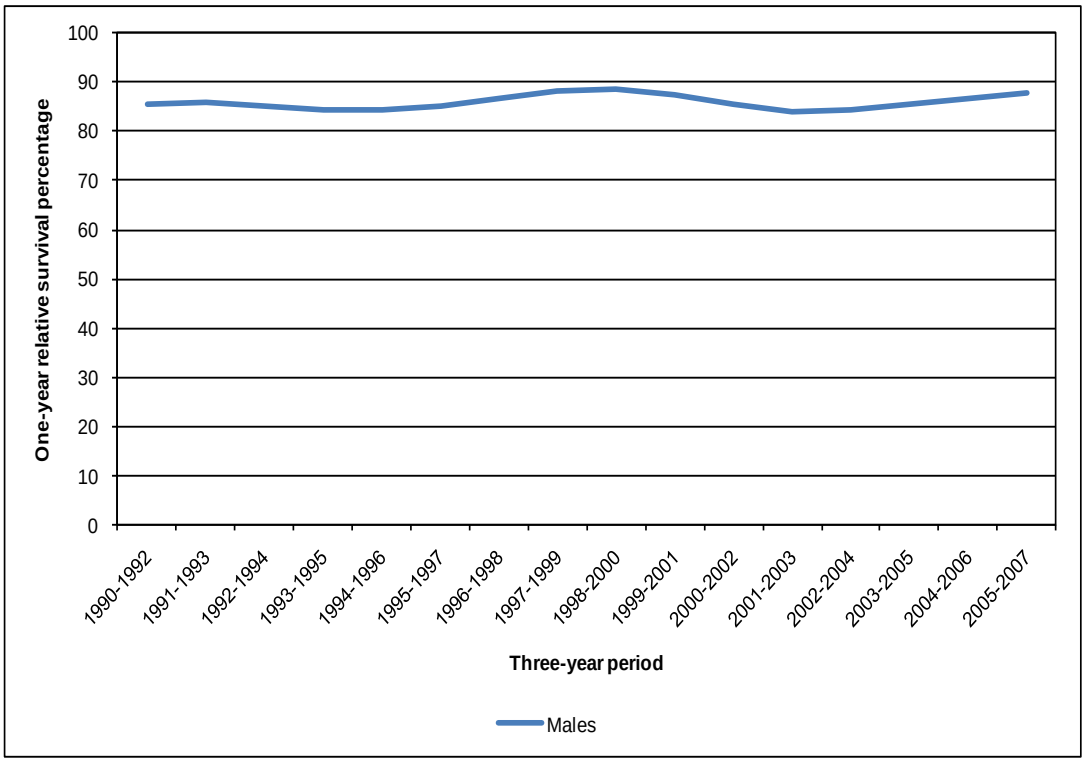
No deaths due to PIN were recorded during the twenty-year period, 1990-2009 analysed in this report.

6. Survival rates

6.1 Penile cancer (ICD10 C60)

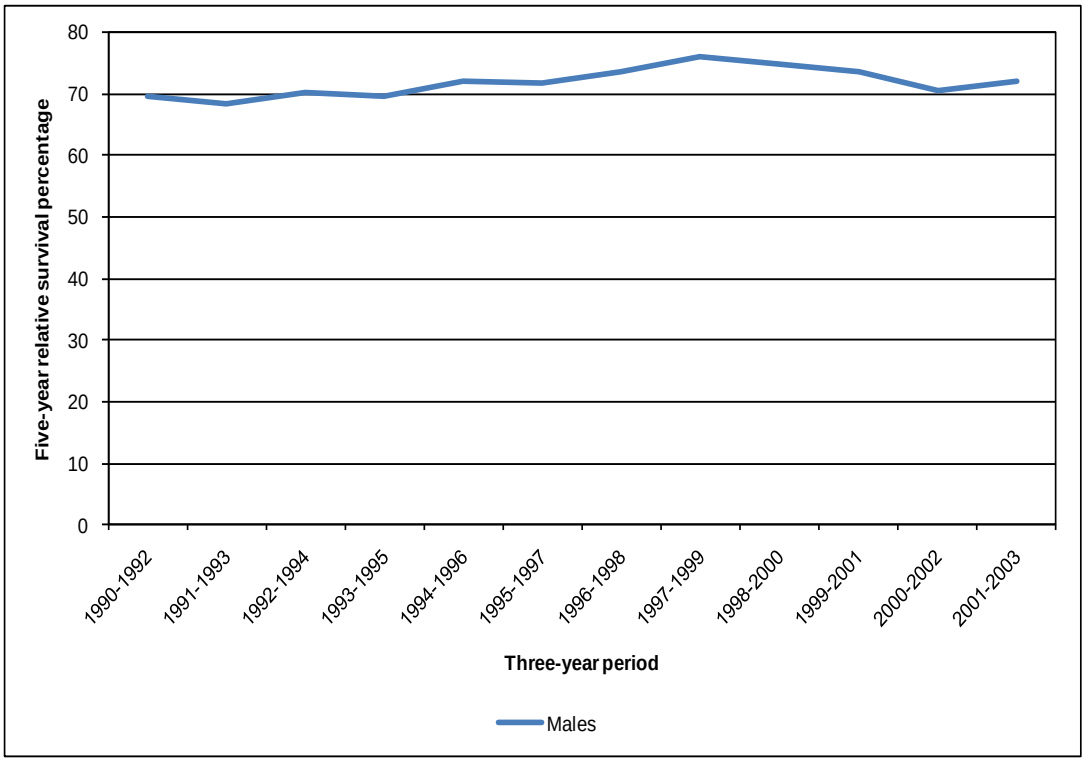
One-year relative survival did not change significantly from 1990-92 to 2005-07. One-year relative survival was 86% from 1990-92 and 88% from 2005-07 (Figure 3). Five-year relative survival also did not change significantly when comparing 1990-92 with 2001-03, with five-year relative survival from 1990-92 being 70% and from 2001-03 being 72% (Figure 4).

Figure 13: One-year relative survival rate (%) for penile cancer (ICD-10 C60), for males, England 1990–2007



Source: South West Public Health Observatory from National Cancer Information Service

Figure 14: Five-year relative survival rate (%) for penile cancer (ICD-10 C60), for males, England 1990–2003



Source: South West Public Health Observatory from National Cancer Information Service

7. Treatments

Treatment modalities, over the most recent 5 years of data available, 2005-09, show surgery is the most common curative treatment option for both penile cancer and PIN. Of a total of 2,030 penile cancers diagnosed during this period 87% of these tumours were treated with surgery. Six percent of penile cancers received radiotherapy and 5% received chemotherapy. It should be noted that recording of radio-, chemo- and hormone therapy is known not to be complete so care should be taken when interpreting these findings.

Of the 650 PIN tumours diagnosed between 2005-09, 66% were treated with surgery and 3% were recorded as receiving chemotherapy. No in-situ tumours are recorded as having received radio or hormone therapy.

Of all malignant tumours, 85% of tumours received at least one of the treatment modalities. The figure for the in-situ penile tumours is 68%.

Note: Percentages may not add to 100% as treatment modalities are not mutually exclusive.

7.1 All modalities

Figure 15: Treatment modalities received for penile cancer diagnosed in England, 2005-2009

	C60 - Penile cancer	
Treatment	**Number**	**%**
Surgery (NCDR)	1,670	82
Surgery (HES)	1,760	87
Radiotherapy	115	6
Chemotherapy	105	5
Hormone Therapy	4	0
Any Treatment*	1,725	85
Total Tumours	2,030	-

Source: National Cancer Data Repository, Hospital Episode Statistics

* National Cancer Data Repository

Figure 16: Treatment modalities received for penile intraepithelial neoplasia diagnosed in England, 2005-2009

	D074 - Penile intraepithelial neoplasia	
Treatment	**Number**	**%**
Surgery (NCDR)	431	66
Surgery (HES)	379	58
Radiotherapy	-	-
Chemotherapy	22	3
Hormone Therapy	-	-
Any Treatment*	444	68
Total Tumours	650	

7.2 Penile Specific Surgeries

Patient treatment pathways were examined for the presence of penile-specific surgical OPCS codes (N26 – N32), which were grouped as follows:

Figure 17: OPCS penile surgical treatment codes and groupings as used in this report

Procedure Category	OPCS Code	Description
Total amputation of penis	N261	Total amputation of penis
Partial amputation of penis	N262	Partial amputation of penis
Partial amputation of penis	N268	Other specified amputation of penis
Partial amputation of penis	N269	Unspecified amputation of penis
Excision of lesion of penis	N271	Excision of lesion of penis
Excision of lesion of penis	N272	Cauterisation of lesion of penis
Excision of lesion of penis	N273	Destruction of lesion of penis NEC
Excision of lesion of penis	N274	Extracorporeal shockwave lithotripsy to lesion of penis
Excision of lesion of penis	N278	Other specified extirpation of lesion of penis
Excision of lesion of penis	N279	Unspecified extirpation of lesion of penis
Reconstruction	N281	Construction of penis
Reconstruction	N282	Reconstruction of penis
Other Operation of Penis	N283	Plication of corpora of penis
Other Operation of Penis	N284	Frenuloplasty of penis
Other Operation of Penis	N285	Correction of chordee of penis
Other Operation of Penis	N286	Repair of fracture of penis
Reconstruction	N287	Graft to penis
Other Operation of Penis	N288	Other specified plastic operations on penis
Other Operation of Penis	N289	Unspecified plastic operations on penis
Other Operation of Penis	N291	Implantation of prosthesis into penis
Other Operation of Penis	N292	Attention to prosthesis in penis
Other Operation of Penis	N298	Other specified prosthesis of penis
Other Operation of Penis	N299	Unspecified prosthesis of penis
Other Operation of Penis	N301	Prepuceplasty
Other Operation of Penis	N302	Freeing of adhesions of prepuce
Other Operation of Penis	N303	Circumcision
Other Operation of Penis	N304	Dorsal slit of prepuce
Other Operation of Penis	N305	Stretching of prepuce
Other Operation of Penis	N306	Manual reduction of prepuce
Other Operation of Penis	N308	Other specified operations on prepuce
Other Operation of Penis	N309	Unspecified operations on prepuce
Other Operation of Penis	N321	Biopsy of lesion of penis
Other Operation of Penis	N322	Drainage of penis
Other Operation of Penis	N323	Incision of penis NEC
Other Operation of Penis	N324	Injection of therapeutic substance into penis
Other Operation of Penis	N325	Removal of constricting object from penis
Other Operation of Penis	N326	Operations on penis for erectile dysfunction NEC
Other Operation of Penis	N328	Other specified other operations on penis
Other Operation of Penis	N329	Unspecified other operations on penis

The most common specific surgical procedure received by men with penile cancer was partial amputation of the penis and for PIN was excision of lesion of penis. There is no specific OPCS code for glansectomy, which is the most common procedure for a localised lesion of the glans or for PIN, and many of these will be coded under a generic excision code.

Figure 18: Penile specific surgeries received for penile cancer diagnosed in England, 2005-2009

	C60 - Penile cancer	
Treatment**	**Number**	**%**
Total Amputation of Penis	215	11
Partial Amputation of Penis	836	41
Excision of Lesion of Penis	669	33
Reconstruction	411	20
Other Operations of Penis	1,418	70
Any Surgery	1,760	87
Total Tumours	2,030	

Source: National Cancer Data Repository, Hospital Episode Statistics

Figure 19: Penile specific surgeries received for penile intraepithelial neoplasia diagnosed in England, 2005-2009

	D074 - Penile intraepithelial neoplasia	
Treatment**	**Number**	**%**
Total Amputation of Penis	1	0
Partial Amputation of Penis	30	5
Excision of Lesion of Penis	211	32
Reconstruction	47	7
Other Operations of Penis	282	43
Any Surgery	379	58
Total Tumours	650	

Source: National Cancer Data Repository, Hospital Episode Statistics

7.3 Time between partial and full amputation

Between 2005 and 2009 only 32 tumours, all malignant, received both and a partial and total amputation. This could indicate that a partial amputation was attempted first, but upon pathological investigation, the margins were found not to be clear so a total amputation was carried out at a later date. The majority of tumours, 47%, received a total amputation over 6 months after a partial amputation.

Figure 20: Time between partial and full amputation of penis for penile cancer diagnosed in England, 2005-2009 (for those patients who have received both types of surgery)

	C60 - Penile cancer	
Treatment*	**Number**	**%**
<0	-	-
Same Day	-	-
1-28 Days	1	3
1-3 Months	9	28
3-6 Months	7	22
> 6 Months	15	47
Total Both Treatments	32	2
Total Tumours	2,030	

Source: National Cancer Data Repository, Hospital Episode Statistics

7.4 Time between partial amputation and reconstruction

A total of 239 penile cancers and 14 PIN received both a partial amputation and some form of reconstructive surgery (12% and 2% respectively). For both malignant and in situ cancers the majority received the partial amputation and reconstruction on the same day (92% and 100% respectively). Data on PIN are not shown as the numbers are too small to analyse.

Figure 21: Time between partial amputation of penis and reconstruction (plastic procedure) for penile cancer diagnosed in England, 2005-2009 (for those patients who have received both types of surgery)

	C60 - Penile cancer	
Treatment*	**Number**	**%**
Same Day	220	92
1-28 Days	1	0
1-3 Months	3	1
3-6 Months	2	1
> 6 Months	13	5
Total Both Treatments	239	12
Total Tumours	2,030	

Source: National Cancer Data Repository, Hospital Episode Statistics

7.5 Time between full amputation and reconstruction

A total of 24 men who had penile cancer were recorded as having a full amputation, and only one man with PIN. Of the 24 men with penile cancer, 17 had a reconstruction date before full amputation. This is likely to be due to reconstruction after a partial amputation, then later recurrence of the cancer requiring a total amputation, as 20 of these men also had a record of partial amputation.

7.6 Total amputation of penis by income deprivation

For PIN there has only been one total amputation of the penis that has taken place over the most recent five year period. This is excluded from analysis.

Men with malignant tumours in the most deprived quintile receive a significantly higher proportion of total amputations than men in any other group (13.9%; $p < 0.05$). There is also a higher proportion in the two most deprived groups combined, when compared to the two least deprived groups combined ($p<0.05$). This implies a deprivation gradient for total amputation towards the most deprived men.

Figure 22: Number of patients who have received a total amputation of the penis for penile cancer diagnosed in England, by deprivation quintile 2005-2009

	Total Amputation		No Amputation	
Quintile ID2007	Number	%	Number	%
1 - Least Deprived	36	9.4	346	90.6
2	35	8.8	362	91.2
3	40	10.3	350	89.7
4	46	10.4	398	89.6
5 - Most Deprived	58	13.9	359	86.1

Source: National Cancer Data Repository, Hospital Episode Statistics

7.7 Partial amputation of penis by income deprivation

For PIN there have only been 30 partial amputations of the penis in the most recent five year period. There is insufficient statistical power to examine any correlation between deprivation and likelihood of partial amputation. For men with penile cancer, the number of partial amputations of the penis show no significant difference between deprivation quintiles, $p = 0.33$.

Figure 23: Number of patients who have received a partial amputation of the penis for penile cancer diagnosed in England, by deprivation, 2005-2009

	Partial Amputation		No Amputation	
Quintile ID2007	Number	%	Number	%
1 - Least Deprived	149	39.0	233	61.0
2	161	40.6	236	59.4
3	166	42.6	224	57.4
4	197	44.4	247	55.6
5 - Most Deprived	163	39.1	254	60.9

Source: National Cancer Data Repository, Hospital Episode Statistics

7.8 Reconstruction by income deprivation

For men with penile cancer, there is no significant difference in reconstruction rates for different income deprivation quintiles. There were only 16 reconstructions for PIN so it is not feasible to analyse.

Figure 24: Number of patients who have received a total or partial amputation of the penis and a reconstruction, for penile cancer diagnosed in England, by deprivation quintile, 2005-2009

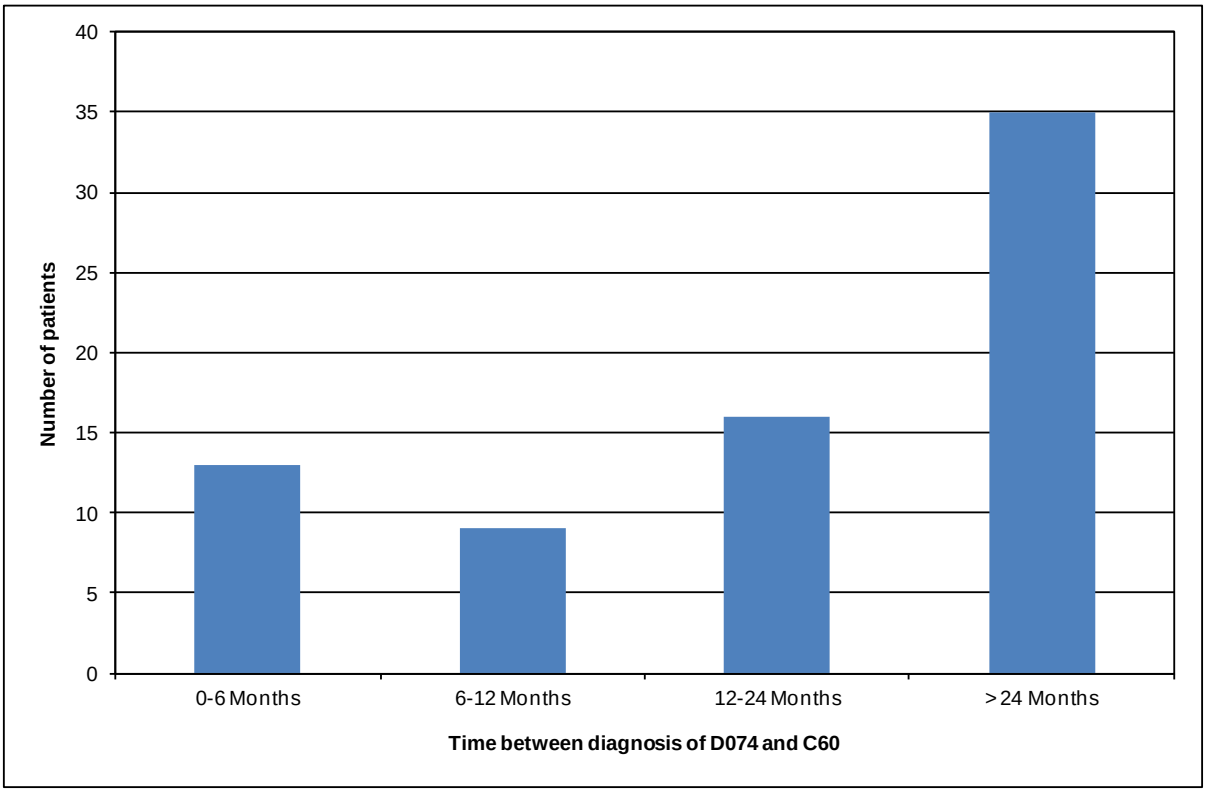
	Reconstruction		No Reconstruction	
Deprivation Quintile	**Number**	**%**	**Number**	**%**
1 (Least deprived)	41	19.3	212	80.7
2	48	20.3	237	79.7
3	50	25.0	200	75.0
4	56	29.6	189	70.4
5 (Most deprived)	48	26.5	181	73.5

Source: National Cancer Data Repository, Hospital Episode Statistics

8. Development of malignancy from penile intraepithelial neoplasia disease

Progress from PIN to penile cancer can occur but tends to take many years to develop. However it is also possible for these conditions to arise separately and independently from each other - either as a synchronous or metachronous lesion. A total of 83 individuals were diagnosed with both PIN and a penile cancer during the study period 1990-2009, an average of approximately 8 men per year. 10 of these men had a diagnosis of penile cancer before PIN, indicating that these were independent lesions rather than progression. 13 men had diagnoses in 0-6 months some of which are likely to be synchronous development of lesions.

Figure 25: Number of patients who have been diagnosed with both penile intraepithelial neoplasia and penile cancer, in England, 1990-2009



Source: National Cancer Data Repository

9. Management of lymph nodes

The optimal management of the pelvic lymph nodes in penile cancer patients has been debated because of the morbidity associated with lymph node excision (Heyns, 2010). However there is also evidence of increased survival in those patients who have lymph node excision (Leveridge, 2008).

HES records of penile cancer patients were searched for the following groups of OPCS codes:

- T851-T859 Block dissection of lymph nodes
- T871-T879 Biopsy or excision of lymph nodes

In addition the presence of two specific codes to identify inguinal (Z616) and pelvic (O141) lymph nodes was noted. Figure 37 shows the percentages of penile cancer patients and sub-groups with recorded lymph node procedures.

Figure 26: Proportion of penile cancer patients with recorded lymph node procedures, 2005-09

		Lymph node management	
	Total	Number	%
All penile cancer patients	2,030	794	39
Full amputation	215	139	65
Partial amputation	836	400	48
Any amputation	1,019	513	50

Source: National Cancer Data Repository, Hospital Episode Statistics

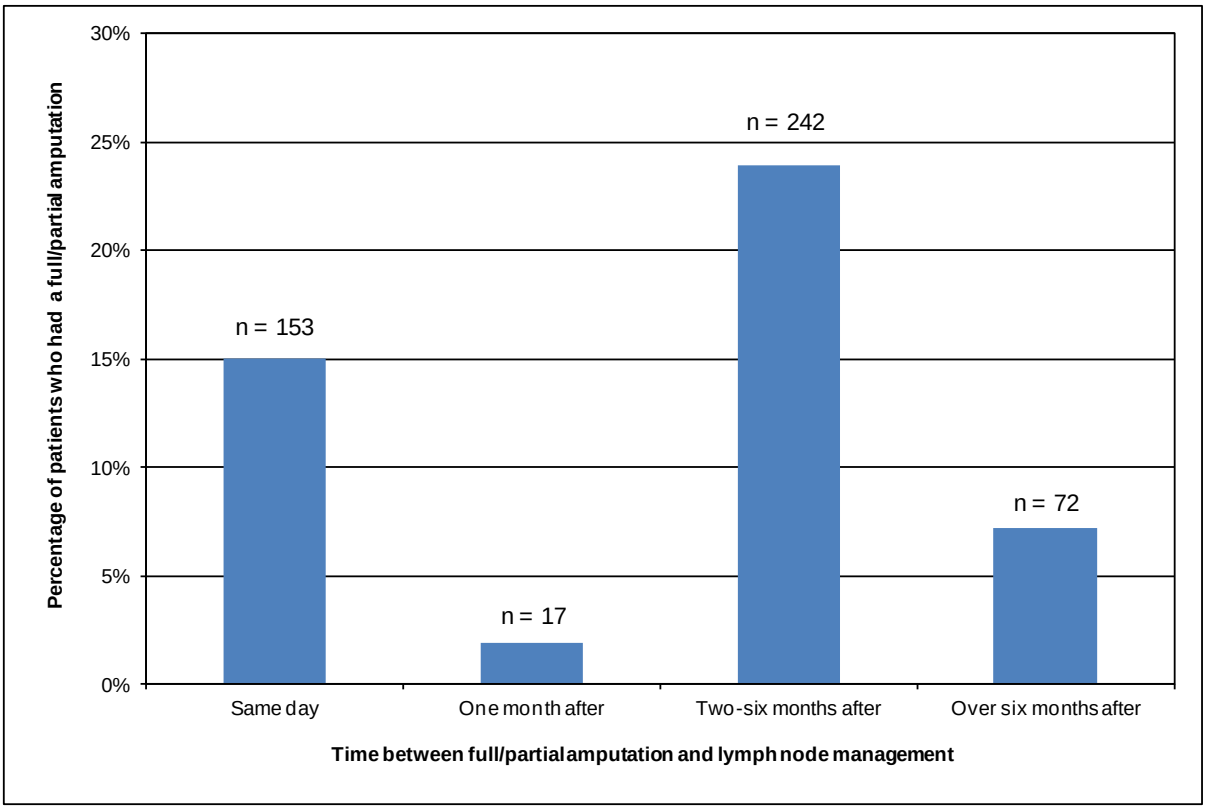
Figure 27: Proportion of penile intraepithelial neoplasia with recorded lymph node procedures, 2005-09

		Lymph node management	
	Total	Number	%
All penile intraepithelial neoplasia patients	650	27	4
Full amputation	1	1	100
Partial amputation	30	5	17
Any amputation	31	6	19

Source: National Cancer Data Repository, Hospital Episode Statistics

For those patients who had a full or partial amputation, the time from amputation to lymph node management was determined. Figure 36 shows the percentage of patients who had a full or partial amputation, who received lymph node management. Many patients (31%) had the lymph node procedure at the same time as their amputation, with a further 52% having the procedure within six months of amputation. There were 11 men (1%) who had lymph node intervention in the month before amputation. These were probably as part of diagnostic and staging investigations.

Figure 28: Proportion of penile cancer/penile intraepithelial neoplasia patients who had a full/partial amputation and recorded lymph node procedures, by time after amputation, 2005-09



Source: National Cancer Data Repository, Hospital Episode Statistics

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The National Cancer Intelligence Network (NCIN) is a UK-wide partnership operated by Public Health England. The NCIN coordinates and develops analysis and intelligence to drive improvements in prevention, standards of cancer care and clinical outcomes for cancer patients.

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