



Cervical cancer

Incidence: case numbers and rate

In the period 2013-2015, invasive cancer of the cervix uteri (ICD10: C53) accounted for just over 1% of all invasive cancers (excluding non-melanoma skin cancer) in Ireland, with an average of 262 cases diagnosed per year. The age-standardised incidence rate (ASIR) for this period was 10.7 per 100,000 per year (1976 European Standard Population).

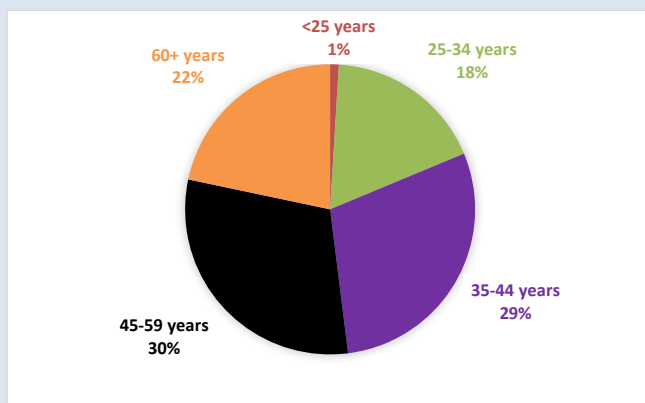
In addition, an annual average of 2,890 cases of carcinoma in-situ of the cervix, ICD10: D06¹ (mainly consisting of cervical intraepithelial neoplasia 3, CIN3), were diagnosed in Ireland during the same period with an ASIR 119 per 100,000.

Age profile

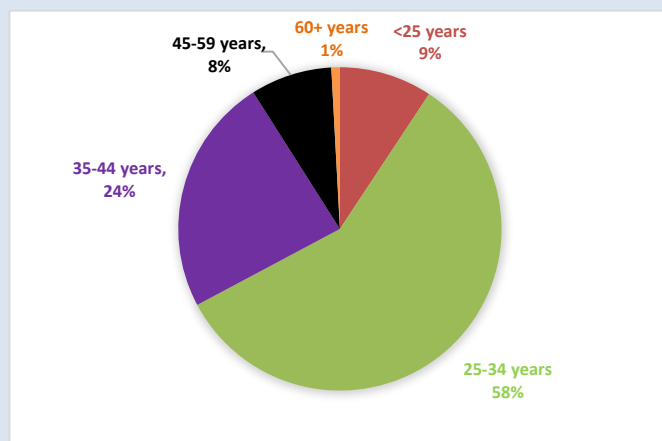
The age profile of invasive cervical cancer is younger than that for many other cancers with almost half (47%) of women aged less than 45 years when diagnosed (Figure 1a).

Figure 1. Age distribution at diagnosis, 1994-2015

(a) Invasive cervical cancer, C53



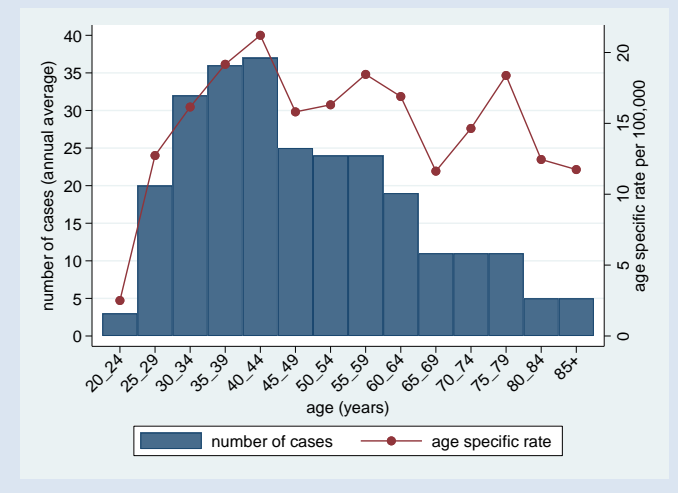
(b) carcinoma in-situ, D06¹



The age profile of women with carcinoma in-situ was even younger with two thirds of women aged less than 35 years at diagnosis (Figure 1b).

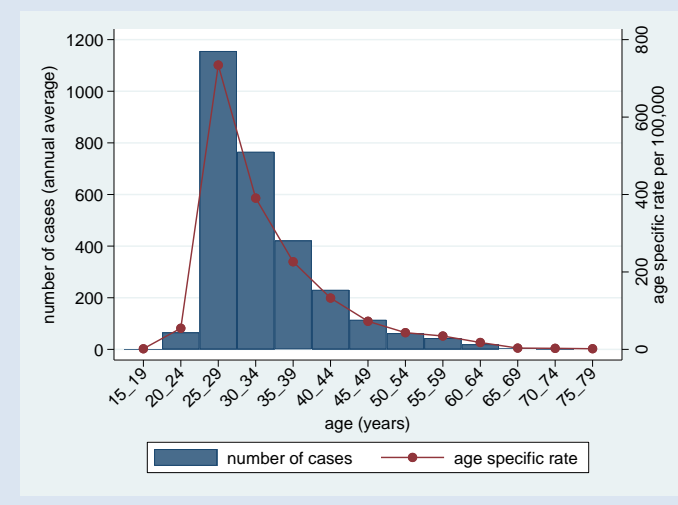
In the period 2013-2015, the greatest numbers of invasive cancers were found in women aged between 35 and 44 years with an annual average of 36/37 cases in the 35-39 and 40-44 age groups respectively and the highest incidence rate was 21.2 per 100,000 for women aged between 40 and 44 years (Figure 2).

Figure 2. Annual average number of cases and age-specific incidence rates 2013-2015, invasive cervical cancer



Incidence rates and case numbers for cervical carcinoma in-situ were highest in women aged 25 to 29 years, with an annual average of 1,156 cases in this age group and an incidence rate of 734 per 100,000 (Figure 3).

Figure 3. Annual average number of cases and age-specific incidence rates 2013-2015, carcinoma in-situ¹

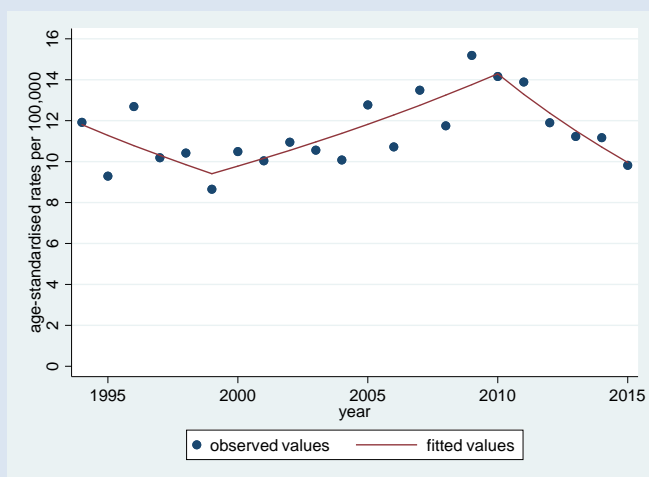


¹ Figures for carcinoma in-situ (D06) include all cases of cervical squamous intraepithelial neoplasia 3 (CIN 3) and adenocarcinoma in situ, but do not include CIN 1/2 cases

Time trends in incidence

Following an initial but non-significant decline in incidence after 1994, there was a significant increase in incidence of invasive cancers in the period 1999-2010 with an annual percentage change (APC) of + 3.9% (95%CI: 1.6%, 6.3%) [1] (Figure 4). There was a significant downward trend, -6.9% (95%CI: -12.4%, -1.2%), in more recent years, 2010-2015, suggesting that the national screening programme, initiated in late 2008 is having an effect on incidence [2].

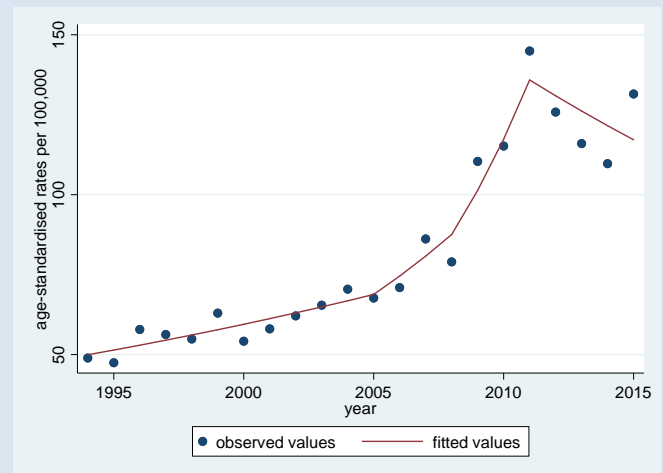
Figure 4. Age-standardised incidence rates, invasive cervical cancer, 1994-2015



period	APC	95% CI
1994-1999	-4.4%	-11.3%, 3.0%
1999-2010	3.9%	1.6%, 6.3%
2010-2015	-6.9%	-12.4%, -1.2%

Incidence of carcinoma in-situ increased at a steady rate of 3.0% (95%CI: 1.1%, 4.9%) per year from 1994 to 2005 and at a faster rate of 8.4% between 2005 and 2008 (Figure 5). This is probably due to increased opportunistic screening over these periods and the influence of a pilot screening programme which commenced in the mid-west region (Clare, Limerick and Tipperary North) in 2001. The national screening programme was consequently rolled out across the whole country in late 2008 and incidence rates subsequently rose considerably, with an APC of 15.8% (95%CI: -2.5, 37.5) between 2008 and 2011. The rates appear to have declined somewhat in more recent years, but further data is required to estimate the longer term trends.

Figure 5. Fitted age-standardised incidence rates, in-situ cervical cancer, 1994-2015

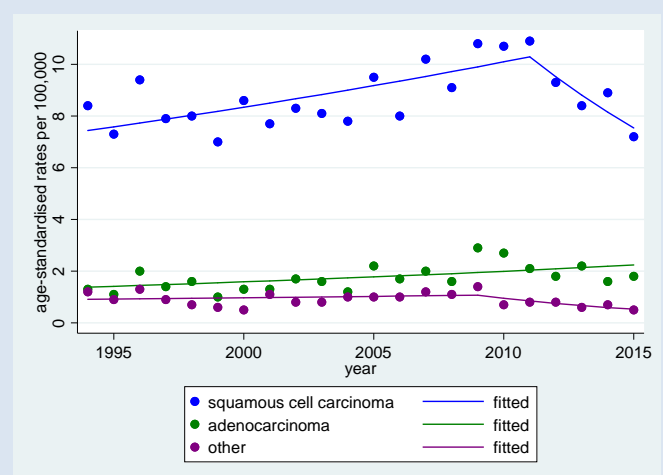


period	APC	95% CI
1994-2005	3.0%	1.1%, 4.9%
2005-2008	8.4%	6.3%, 21.3%
2008-2011	15.8%	-2.5%, 37.5%
2011-2015	-3.6%	-8.6%, 1.6%

Incidence rates by histological types, invasive cervical cancer

Over the entire period, 1994-2015, the proportion of invasive cervical cancers which were classified as squamous cell carcinoma was 77%, while adenocarcinoma made up 16% of these cancers. The remaining 8% consisted of other histological subtypes.

Figure 6. Age-standardised-rates, by histological subtype, cervical cancer



	Period	APC	95% CI
squamous	1994-2011	+1.9%	0.9%, 3.0%
	2011-2015	-7.5%	-15.2%, 0.9%
adenocarcinoma	1994-2015	+2.3%	0.5%, 4.1%
other	1994-2009	+1.1%	-1.5%, 3.8%
	2009-2015	-10.7%	-20.5%, 0.4%

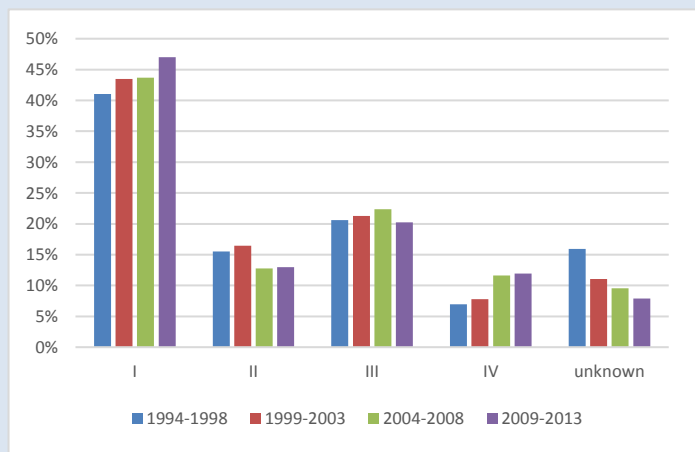
Age-standardised rates of squamous cell cervical cancer rose by an average of 1.9% (95%CI: 0.9%, 3.0%) per year in the period 1994-2010 and then dropped/stabilised from 2011 (Figure 6).

However, adenocarcinoma rates continued to rise over the whole period 1994-2015 by 2.3% per year (95%CI: 0.5%, 4.1%). Cytology screening is not as effective for adenocarcinoma of the cervix as it is for squamous cell carcinoma and rising rates for this type of cervical cancer may be linked to an increase in underlying risk factors in the population, e.g. prevalence of human papillomavirus high risk type 18.

Stage at diagnosis

The stage distribution of cervical cancer has remained reasonably stable over time (Figure 7). It is expected that the introduction of screening would correspond to an increase in early stage cancer. The percentage of stage I cancers increased from 41% in 1994-1998 to 47% in the period 2009-2013. There is an improvement in the staging information, as the proportion of cancers with stage unknown, decreased from 16% in 1994-1998 to 8% 2009-2013.

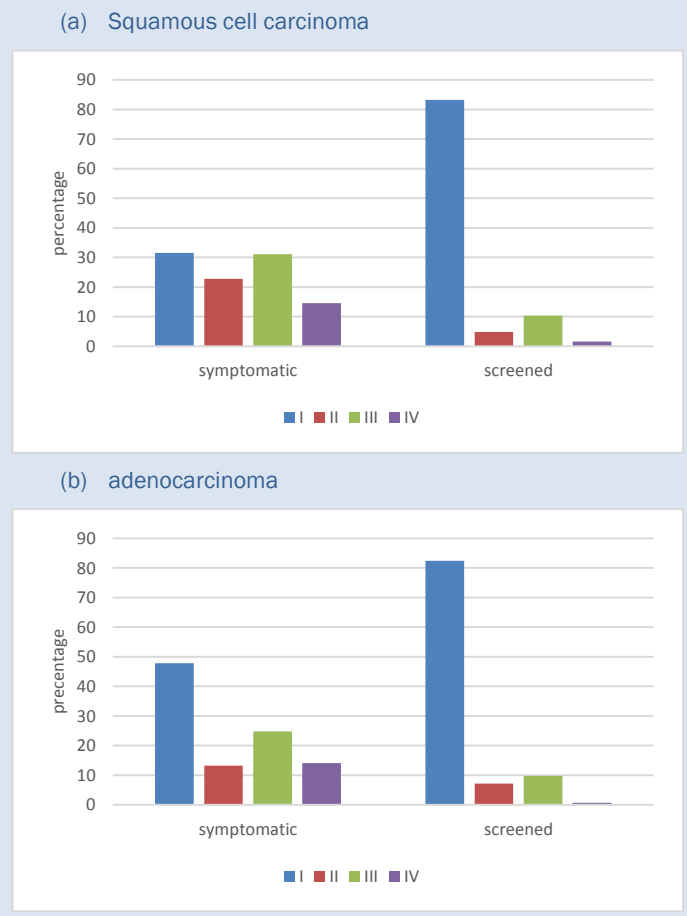
Figure 7. Stage distribution over time, invasive cervical cancer



For women with squamous cell carcinoma (Figure 8a), less than a third (31%) of those who presented symptomatically had stage I cervical cancer, while 83% of those who presented through screening had a stage I tumour.

We see a similar effect for women with adenocarcinoma (Figure 8b). Nearly half (48%) of those presenting symptomatically had a stage I tumour, while 83% of those presenting through screening had a stage I tumour.

Figure 8. Stage distribution of invasive cervical cancer by method of presentation, 1994-2015



Social class and incidence

Patients were assigned to an area-based deprivation category derived from census variables [3]. The most deprived areas had very clearly the highest burden of invasive cervical cancer incidence (> the 20% of cases expected from the general population distribution), and this has remained constant over time (Figure 9). There was relatively little variation in the relative proportions of cases across the other four deprivation categories but a slight increase with deprivation was observed. It remains to be seen whether further screening and the HPV vaccine will have any impact on the socio-economic distribution of cases.

Figure 9. Percentage of cervical cancer cases by deprivation class (population quintiles).

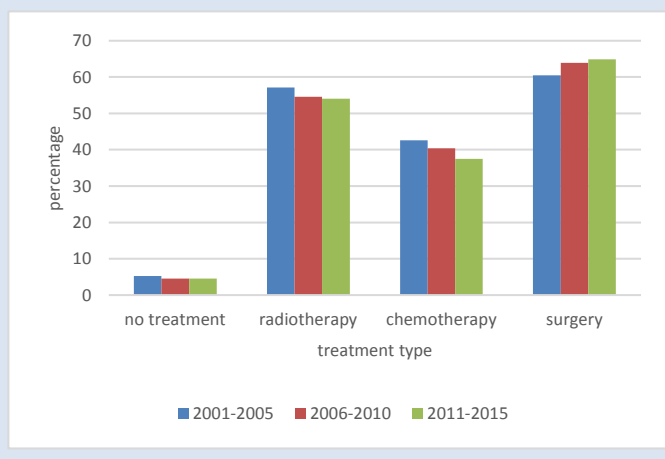


Treatment

In the fifteen year period from 2001 to 2015 inclusive, 63% of women had surgery (ranging from 60% in 2001-2005 to 65% in 2011-2015) (Figure 10). These figures include conization (cone biopsy), but do not include women who had other types of biopsy with no further surgery; however, for smaller lesions the biopsy procedure can remove the tumour, completely eliminating the need for further surgery.

Chemotherapy was administered to 40% of patients overall, with a slight decline over time from 43% in 2001-2005 to 38% in 2011-2015. The proportion receiving radiotherapy also decreased slightly, from 57% in 2001-2005 to 54% in 2011-2015. Very few women (approximately 5%) had no tumour-directed treatment.

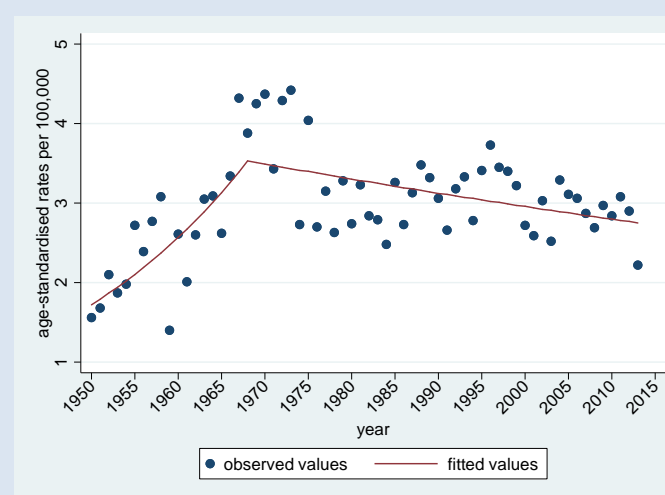
Figure 10. Percentage of patients receiving treatment for cervical cancer, during the 15 year period 2001-2015.



Mortality

Mortality rates for cervical cancer increased significantly in Ireland from 150 in the late 1960s but have been in fairly constant decline since 1969, with an annual percentage change of -0.6% per year (95%CI: -0.9%, -0.2%) (Figure 11).

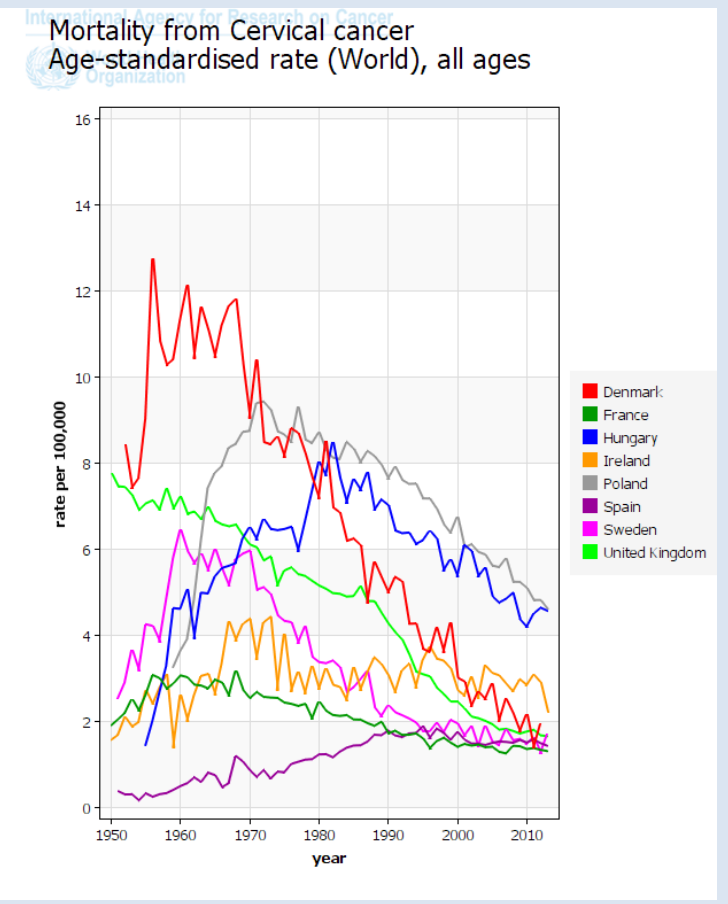
Figure 11. Age-standardised mortality rates (world) for cervical cancer, Ireland, 1950 - 2013 [4].



period	APC	95% CI
1950 - 1969	4.1%	2.5%, 5.6%
1969 - 2013	-0.6%	-0.9%, -0.2%

Comparing Ireland to other countries in Europe, we see that the decreasing trend was steeper in other countries, though some (e.g. Denmark, Hungary and Poland) had much higher rates initially (Figure 12) [4]. Recent mortality rates in Hungary and Poland are higher than those in other countries, including Ireland, where current rates are all fairly similar at approximately 2 deaths per 100,000 per year.

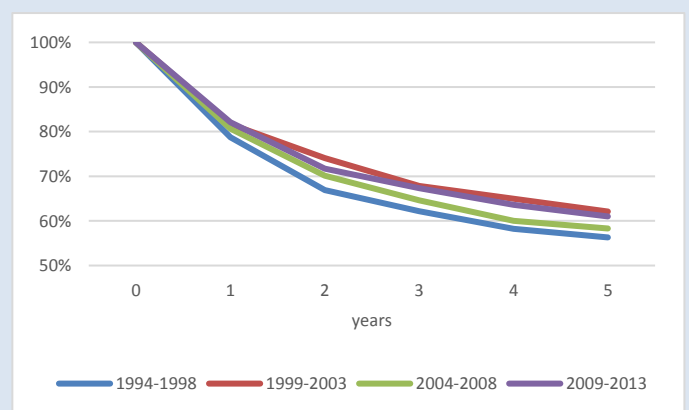
Figure 12. Mortality trends, cervical cancer for selected European countries [4]



Survival

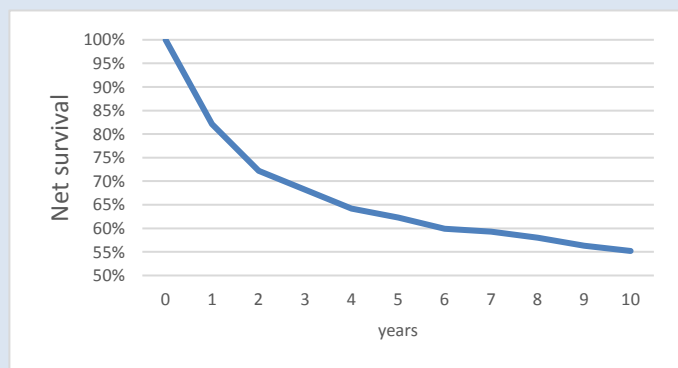
Net survival for cervical cancer at five years was 56% in the period 1994-1998, 62% in the period 1999-2003, 58% in 2004-2008 and 61% in 2009-2013, showing relatively stable survival trends over time (Figure 13).

Figure 13. Five-year net survival for cervical cancer, comparing four diagnosis periods from 1994 to 2013



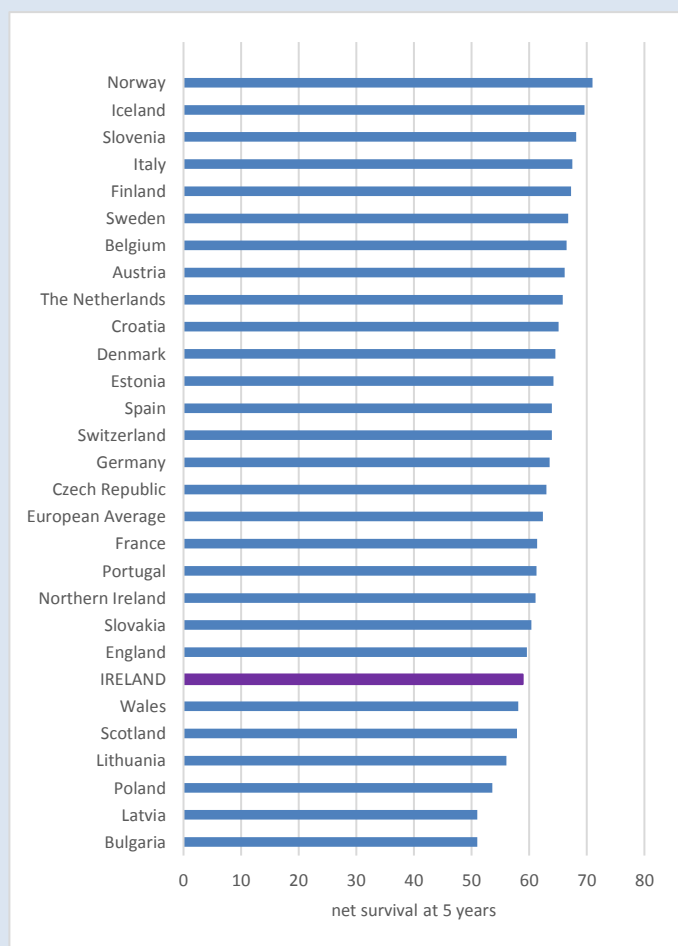
Looking at survival for the most recent five-year period (2009-2013), there was a continuous but slow decline in net survival with age to a ten-year net survival of 55%, indicating survival had not yet reached an equilibrium i.e. returned to that expected in the general population (“population cure”), even after ten years (Figure 14).

Figure 14. Ten-year net survival for cervical cancer in the period 2010-2014



Data from the EUROCARE-5 database [5] for the period 2000-2007 indicated that the five-year survival from cervical cancer in Ireland at 59% was below the European average of 62%, but similar to Scotland and Wales (58%) and England at almost 60% (Figure 15).

Figure 15. Five-year net survival for cervical cancer, 2000-2007



REFERENCES

[1] H. J. Kim, M. P. Fay, E. J. Feuer, and D. N. Midthune, “Permutation tests for joinpoint regression with applications to cancer rates,” Stat. Med., vol. 19, no. 3, pp. 335–351, Feb. 2000.

[2] The national cervical screening programme website: <https://www.cervicalcheck.ie/>

[3] Haase T, Pratschke J. The Pobal-Haase deprivation index for small areas. Pobal, Dublin. 2010. <https://maps.pobal.ie/WebApps/DeprivationIndices/index.html>

[4] Data extracted from the WHO database (<http://www.dep.iarc.fr/WHOdb/WHOdb.htm>). Note rates are standardised to the world standard population.

[5] Survival of cancer patients in Europe – the EUROCARE-5 study, figures extracted from the online database: <https://w3.iss.it/site/EU5Results/forms/SA0007.aspx>