

Survival from cervical cancer in Barshi registry, rural India

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Introduction

The first rural population-based cancer registry in India was established in 1987 in Barshi, in the state of Maharashtra in western India, as part of the National Cancer Registry Programme of the Indian Council of Medical Research, Government of India. The need for data on cancer incidence from rural areas of India had long been recognized, as more than 75% of the Indian population lives in rural areas. A realistic estimate of the national cancer burden is therefore possible only if rural cancer incidence is documented. Before the establishment of the Barshi registry, the incidence of cancer in rural areas of the country was estimated by undertaking ad hoc surveys in selected areas, at considerable cost in both money and time (Wahi, 1968; Jayant *et al.*, 1975; 1976; Gupta *et al.*, 1980). In recent years, more

rural cancer registries have been, or are now being, established in different parts of the country.

The Barshi cancer registry covers the rural areas of Barshi, Paranda and Bhum *tahsils* (a *tahsil* is an administrative structure equivalent to a subdistrict), with 346 villages spread over an area of 3713.4 km² in Maharashtra state, about 600 m above sea level and 400 km south-east of Bombay (Fig. 1). The village is the basic administrative unit in nonurban areas of India. Barshi *tahsil* is in Solapur district, and Paranda and Bhum *tahsils* are in Osmanabad district. The literacy level ranges from 30% to 44% in different regions of the registry area, although efforts are being made to improve it, with primary schools now established in every village.

In this chapter, we describe the population-based survival experience of cervical cancer patients in Barshi registry, and discuss the implications of the results in the context of cancer control.

Cancer registration in Barshi registry

Cancer registration in rural areas of India poses a number of challenges. Lack of medical facilities, a low literacy rate, lack of cancer awareness, poor referral practices, poor quality of records and a number of other constraints make it difficult to achieve adequate coverage of cases. We have developed a unique method of case-finding to overcome these deficiencies (Jayant *et al.*, 1989, 1991, 1995).

Case identification is undertaken by trained investigators, who visit the allotted villages at least once every six months to collect information on proven/likely cases as well as chronically ill persons. They contact all medical practitioners in the area and meet health workers from the local primary health centres at their monthly meetings. They hold group meetings to improve cancer awareness among the villagers. They also visit every tenth household in the



Figure 1. Map showing location of Barshi

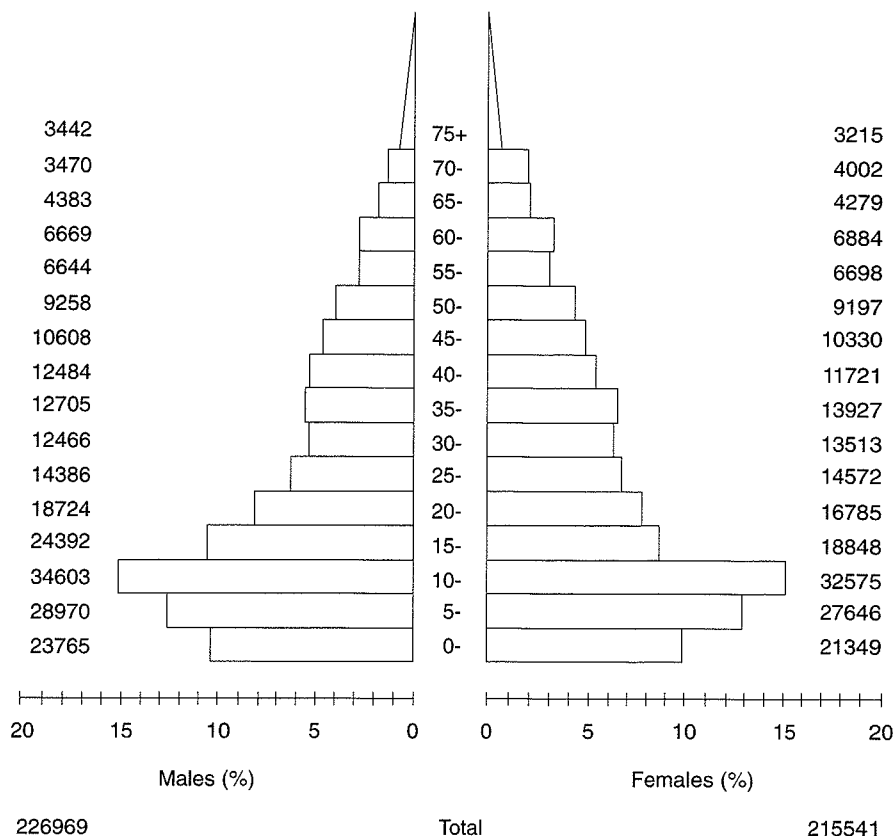


Figure 2. Average annual population of Barshi, 1988–92

village to enquire about proven or likely cancer cases. They give a referral card to any people with suspected cancer and ask them to attend the cancer hospital at Barshi quickly or to visit the opportunistic cancer detection clinics conducted in their vicinity at regular intervals. People who do not comply are revisited to ascertain whether the symptoms have persisted and to encourage them to seek medical attention.

The registry staff regularly visit hospitals within and outside the registry area ($N=35$), all the primary health centres in the registry area ($N=15$), and the cancer registries of Bombay, Pune and Aurangabad to collect information on cancer cases actively and in a standard format. Deaths are registered in the respective block development and panchayath offices attached to specific villages. Registry staff visit these offices to collect death information in a standard format.

The data collected are checked for completeness, duplicates are eliminated by visual inspection

of registry lists, and the data are coded using the National Cancer Registry Programme manual (National Cancer Registry Programme, 1987). The primary site and histology are coded using the *International Classification Of Diseases For Oncology*, First Edition codes (WHO, 1976). *International Classification of Diseases, Ninth Revision (ICD-9)* codes are used for reporting purposes (WHO, 1978).

The population of each village in the registry area by sex is listed in the ten-yearly census reports issued by the state of Maharashtra. Age-sex distributions are estimated on the basis of sample surveys in each district. The population structure of the registry for the mid-period of 1988–92 is shown in Fig. 2. The total population is 0.4 million and the sex ratio is 950 females to every 1000 males. The proportion of people under 15 years of age is 38.2%, and that of people over 64 years is 5.2%.

The incidence data from the registry have been published in annual reports (Jayant *et al.*, 1989, 1991,

Table 1. Annual average cancer incidence per 100 000 person-years in Barshi registry, India, 1988–92

Site	MALES			FEMALES		
	Number	Crude rate	ASR	Number	Crude rate	ASR
Lip	3	0.3	0.3	0		
Tongue	19	1.7	2.3	3	0.3	0.3
Salivary gland	4	0.4	0.5	1	0.1	0.1
Mouth	33	2.9	3.8	7	0.6	0.8
Oropharynx	6	0.5	0.8	1	0.1	0.1
Nasopharynx	0			0		
Hypopharynx	56	4.9	6.7	5	0.5	0.5
Oesophagus	49	4.3	5.8	16	1.5	1.9
Stomach	7	0.6	0.8	8	0.7	0.9
Colon	6	0.5	0.7	4	0.4	0.4
Rectum	23	2.0	2.6	10	0.9	1.1
Liver	15	1.3	1.8	6	0.6	0.7
Gallbladder	1	0.1	0.1	2	0.2	0.2
Pancreas	4	0.4	0.5	2	0.2	0.2
Larynx	21	1.9	2.5	0		
Lung	11	1.0	1.3	3	0.3	0.3
Bone	4	0.4	0.3	5	0.5	0.5
Connective tissue	6	0.5	0.5	2	0.2	0.2
Melanoma of skin	0			1	0.1	0.1
Other skin	12	1.1	1.4	10	0.9	1.1
Breast	0			78	7.2	8.7
Cervix uteri				252	23.4	27.4
Corpus uteri				3	0.3	0.3
Ovary				12	1.1	1.2
Prostate	12	1.1	1.4			
Testis	3	0.3	0.3			
Penis	29	2.6	3.3			
Bladder	9	0.8	1.0	0		
Kidney	4	0.4	0.4	1	0.1	0.1
Brain	4	0.4	0.4	2	0.2	0.2
Thyroid	5	0.4	0.5	2	0.2	0.2
Hodgkin's disease	5	0.4	0.4	0		
Non-Hodgkin lymphoma	9	0.8	1.0	5	0.5	0.6
Multiple myeloma	1	0.1	0.1	1	0.1	0.1
Lymphoid leukaemia	9	0.8	0.7	6	0.6	0.5
Myeloid leukaemia	10	0.9	1.1	5	0.5	0.4
All sites	453	39.9	51.8	502	46.6	55.0
All sites except skin	441	38.9	50.4	492	45.7	53.9

ASR: Age-standardized incidence rate (world population)

1996a), in reports of the Indian Council of Medical Research (National Cancer Registry Programme, 1992) and in Volume VII of *Cancer Incidence in Five Continents* (Parkin *et al.*, 1997). A preliminary report on the observed survival of cervical cancer patients registered during the period 1988–91 was published recently (Jayant *et al.*, 1996b).

Cancer incidence in Barshi registry

In terms of overall cancer incidence, 453 cases among males and 502 cases among females were

registered in the period 1988–92. The average annual age-standardized incidence rates per 100 000 population were 51.8 for males and 55.0 for females (Table 1). These are less than half the rates observed in urban populations in India (Parkin *et al.*, 1997). Though underdiagnosis and under-registration may account for the lower rates, a genuine low risk for many cancer sites is a distinct possibility, given the differences in lifestyle and other exposures.

Among males, cancers of the hypopharynx, oesophagus, mouth and penis have the highest incidence rates, accounting for more than one-third

Table 2. Cases of cancer registered and data quality indices, Barshi registry, India, 1988–92

Site	ICD 9	No. of cases registered	Data quality indices		Cases excluded from analysis		Cases included for survival analysis	
			% DCO	% HV	DCO	Others	No.	%
Cervix	180	252	0.0	92.5	0	5	247	98.0

DCO : Death certificate only; HV : Histological verification

Table 3. Observed and relative survival by site and sex, Barshi registry, India, 1988–92

Site	ICD 9	Number included	All ages					
			Observed survival			Relative survival		
			1 yr	3 yr	5 yr	1 yr	3 yr	5 yr
Cervix	180	247	62.8	36.2	30.9	63.7	37.9	33.3

of all cancers. There is a high risk of hypopharyngeal cancer in western India, as indicated by high rates in Bombay (Parkin *et al.*, 1997) and Ahmedabad (Parkin *et al.*, 1992).

Among females, there is a high risk of cervical cancer (age-standardized incidence rate (ASR) 27.4/100 000), accounting for half of all female cancers. It is likely that these are underestimates of the true risk, because of underdiagnosis and some incompleteness in registration. Preliminary results from a rural cancer registry at Ambalikkai, in South India, indicate an even higher risk of cervical cancer (ASR 47.1/100 000 in 1995–96) among women in rural areas of India (Cherian and Rajkumar, 1997).

Health services

Primary health care delivery is administered through primary health centres and rural hospitals. There is one primary health centre with a medical officer and support staff for about 30 000 people. Under each primary health centre, there are several subcentres in the charge of an auxiliary nurse-midwife and a multipurpose health worker. Besides these workers, there is one community health worker for every 1000 people. There is a total of 15 primary health centres, 18 rural hospitals, 76 subcentres, 140 medical practitioners and 550 health workers in the registry area.

A voluntary body (the Ashwini Rural Cancer Research and Relief Society) took the initiative of setting up a comprehensive cancer hospital (Nargis Dutt Memorial Cancer Hospital), in the rural environs of Barshi, to serve the needs of the rural population. This hospital is now fully equipped to

carry out histopathological, cytological, radiological and surgical procedures for cancer diagnosis and provides cancer surgery, radiotherapy, chemotherapy and palliative care.

Early detection

As already indicated, one of the registry's methods of case-finding is to promote awareness of cancer risk factors and symptoms among the rural population and to encourage early detection behaviours. The registry area is divided into 12 zones, each covering approximately 30 villages. Opportunistic detection clinics are conducted twice a year in each zone, soon after completion of village visits by the registry staff. To facilitate referrals, a complete list of dates and locations of these detection clinics is given to all medical practitioners, hospitals and primary health centres in the area. The detection clinics are conducted by fully qualified oncologists. Cervical cytology is offered to women attending the clinics.

The results of a pilot population-based study to evaluate the performance of visual inspection in the early detection of cervical cancer, involving the female population of Agalgaon primary health centre area, have been published (Nene *et al.*, 1996).

Survival analysis

Subjects

A total of 252 cervical cancer cases were registered during the period 1988–92 (Table 2). Of these, 92.5% cases had histological verification. Four cases without any follow-up information and one case

Table 4. Age-specific number of cases, five-year relative survival and ASRS, Barshi registry, India, 1988–92

Site	ICD 9	Number of cases by age group						% Relative survival (RS) at 5 years						RS	ASRS%	
		≤34	35–44	45–54	55–64	65–74	75+	≤34	35–44	45–54	55–64	65–74	75+		All ages	0–74
Cervix	180	16	67	68	74	18	4	31.8	39.4	34.5	24.7	28.5	84.7	33.3	38.5	32.0

ASRS: Age-standardized relative survival

without date of diagnosis were excluded, leaving 247 cases for final analysis. Since there was a focus on studies of cervical cancer in this rural population, particular attention was paid to collecting details of histology, staging (using the International Federation of Gynaecologists and Obstetricians (FIGO) system) and treatment.

The distribution of histology was as follows:

- squamous cell carcinoma 219 cases (88.7%)
- adenocarcinoma 10 cases (4.0%)
- histology unknown 18 cases (7.3%).

The stage distribution was as follows:

- stage I 47 cases (19.0%)
- stage II 44 cases (17.8%)
- stage III 113 cases (45.7%)
- stage IV 5 cases (2.0%)
- unknown 38 cases (15.5%).

The treatment details were as follows:

- 104 people (42.1%) had completed prescribed treatment
- 26 people (10.5%) had only partial treatment
- 117 people (47.4%) had no treatment.

Follow-up

The vital status of subjects was mainly established by house visits. At the closing date for follow-up (31 December 1995), 171 (69.2%) subjects were known to be dead, 66 (26.7%) were alive; and 10 (4.1%) had been lost to follow-up.

Analytical methodology (see Chapters 2, 3 and 5)

The index date for calculation of survival time was the incidence date. The survival time for each case was the time between the index date and the date of death *or* date of loss to follow-up *or* 31 December 1995. Cumulative observed and relative survival probabilities were calculated using Hakulinen's method (Hakulinen, 1982; Hakulinen *et al.*, 1994). The expected survival for a group of people in the general population similar to the patient population with respect to age, sex, and calendar period of

observation was calculated using the abridged life tables of the rural Indian population (Registrar General of India, 1995). Age-standardized relative survival (ASRS) rates were calculated for all age groups and for the age group 0–74 years by directly standardizing site-specific and age-specific relative survival to the site-specific age distributions of the estimated global incidence of major cancers in 1985 for comparison with results from other countries.

Since we had reliable information on age, stage and histology, we wished to examine the prognostic importance of these variables for survival. We also divided the period of observation into two periods: 1988–89 and 1990–92. The log rank test (Mantel, 1966) was used to identify significant factors on univariate analysis. These were then entered stepwise into a proportional hazards regression model (Cox, 1972) to identify independent predictors of survival outcome.

Results

The one-year, three-year and five-year observed and relative survival from cervical cancer are shown in Table 3. One-third of patients had survived five years from diagnosis. The age-specific five-year relative survival rates do not indicate any impact of age on survival (Table 4). Table 5 shows observed survival by stage, histology, registration period and treatment, and Figs. 3–5 show the survival outcome until five years from diagnosis according to histology, stage of disease and period of registration, respectively. The five-year survival by histology was 32.1% for squamous cell carcinoma, 20% for adenocarcinoma and 24.7% for those without a histological diagnosis (Fig. 3); survival by FIGO stages was 59.6% for stage I, 31.5% for stage II, 11.6% for stage III, 20% for stage IV and 54.8% for unstaged cancers (Fig. 4). The observed five-year survival was higher for cases diagnosed in 1990–92 than for cases from 1988–89 (Fig. 5).

On univariate analysis, stage, histology and period of registration emerged as significant variables affecting survival outcome. The results of multifactorial analysis, after adjustment for any residual effect of age at incidence date, are given in

Table 5. Observed survival by stage, histology, registration period and treatment, Barshi registry, India, 1988–92

Factor	Number	%	Survival %		
			1 year	3 years	5 years
Stage					
I	47	19.0	95.7	68.1	59.6
II	44	17.8	70.5	43.0	31.5
III	113	45.7	44.2	15.0	11.6
IV	5	2.0	40.0	20.0	20.0
Unknown	38	15.5	71.1	54.8	54.8
Histology					
Squamous cell carcinoma	219	88.7	64.4	37.4	32.1
Adenocarcinoma	10	4.0	40.0	20.0	20.0
Unknown	18	7.3	55.6	32.9	24.7
Registration period					
1988–89	78	31.6	52.6	26.9	24.4
1990–92	169	68.4	67.5	40.6	33.1
Treatment					
Complete	104	42.1	90.4	65.3	54.8
Partial/no details	26	10.5	61.5	17.6	17.6
No treatment & treatment details not known	117	47.4	38.5	14.3	12.6

Table 6. Advanced stage of disease and adenocarcinoma emerged as poor prognostic factors. Cases registered during 1990–92 demonstrated a significantly lower relative risk of death than cases from 1988–89.

Discussion

This is the first comprehensive report of cervical cancer survival in an entirely rural population in India. Every effort has been made to improve opportunities for diagnosis, and to register all diagnosed cases in the population. We are confident that more than 90% of the diagnosed cases of cervical cancer from the area are in our database. Our unique method of active coverage and the rudimentary death registration system in the region explain the absence of DCO cases.

We began to observe a stage shift in diagnosed cases as registration activity progressed, possibly because our case-finding mechanism involved cancer-related health education and early detection initiatives (Jayant *et al.*, 1995). Because of this, we wished to examine the survival of cancer patients registered during 1988–89 and 1990–92, to see whether there were any differences in survival between the two periods (Fig. 5). It is interesting to note that the five-year observed survival for the

second period was significantly higher than for the first: 33.1% versus 24.4% ($p < 0.05$). When this was adjusted for stage distribution, histology and age in a Cox proportional hazards regression analysis, the observed survival difference remained significant (Table 6).

Cases diagnosed during the second period had a favourable stage distribution, and there were differences in treatment as well (Table 7). Sixty percent of patients diagnosed during the first period did not begin or complete treatment, compared with 42% of patients during the second period. It is obvious that health education, plus the opportunities for early detection provided by the unique case-finding mechanism of our registry, improved both stage distribution and compliance with treatment. This seems to be responsible for the better prognosis observed during the second period. Compliance with treatment had a major impact on survival, as shown in Table 5 and Fig. 6.

The five-year observed survival among cervical cancer patients in Barshi (30.9%) is a little lower than that observed in Bangalore (34.4%) (Nandakumar *et al.*, 1995). It is much lower than that reported in a hospital-based study from Trivandrum, India (47.4%) (Sankaranarayanan *et al.*, 1995). Age-standardized relative survival from cervical cancer in Barshi is in the lower half of the

Table 6. Multifactorial analysis of prognostic factors for cervical cancer in Barshi registry, India

Factor	Hazard ratio ¹	95% CI	χ^2 value	p value
Stage			58.1	<0.0001
I	1.0			
II	2.6	1.4–4.6		
III	5.9	3.4–10.0		
IV	4.4	1.2–15.3		
Histology			5.6	<0.05
Squamous cell carcinoma	1.0			
Adenocarcinoma	2.8	1.3–5.9		
Period of registration			4.9	<0.05
1988–89	1.0			
1990–92	0.7	0.4–0.9		

¹After age adjustment

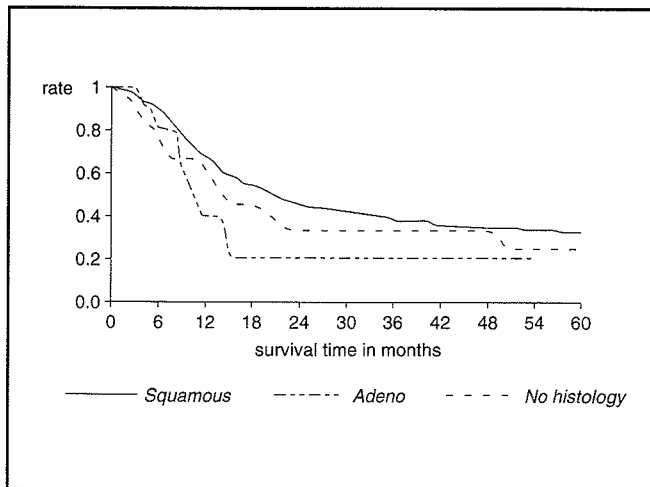


Figure 3. Survival from cervical cancer by histology in Barshi registry, India

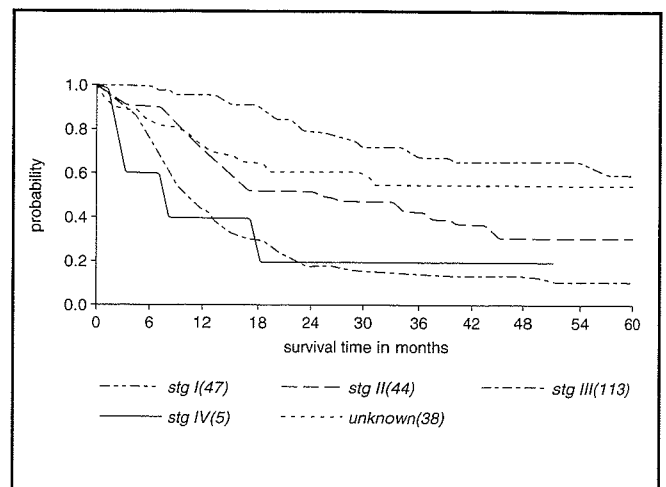


Figure 4. Survival from cervical cancer by stage of disease in Barshi registry, India

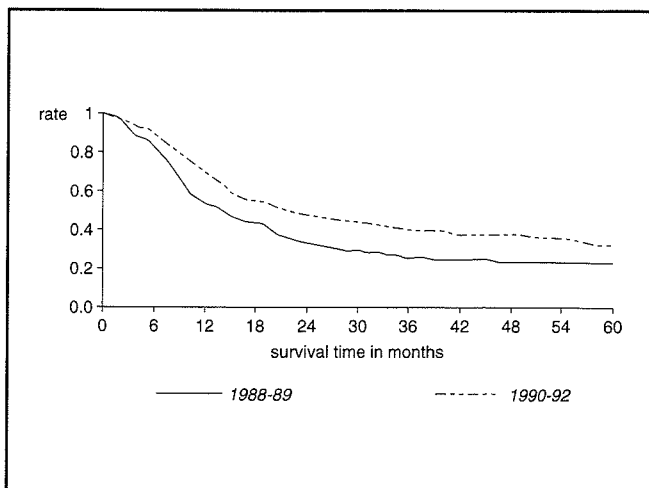


Figure 5. Survival from cervical cancer by period of registration in Barshi registry, India

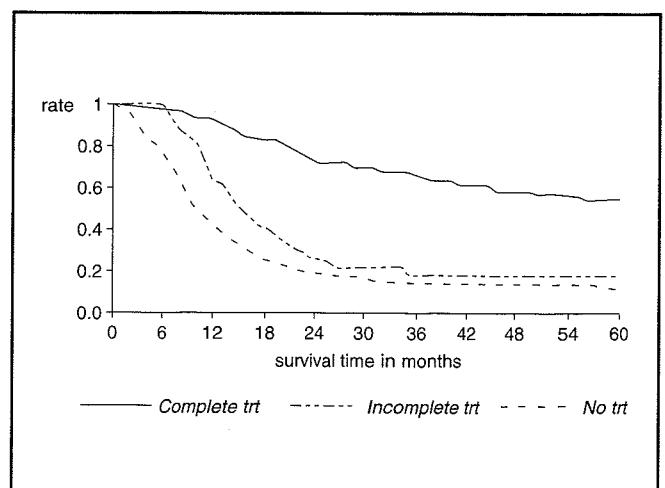


Figure 6. Survival from cervical cancer by treatment in Barshi registry, India

Table 7. Stage and treatment of disease by registration period, Barshi registry, India

Stage (FIGO)	1988-89 (%)	1990-92 (%)	Total (%)
I	12 (15.4)	35 (20.7)	47 (19.0)
II	13 (16.7)	31 (18.3)	44 (17.8)
III	39 (50.0)	74 (43.8)	113 (45.8)
IV	3 (3.8)	2 (1.2)	5 (2.0)
Unknown	11 (14.1)	27 (16.0)	38 (15.4)
Treatment			
Surgery	11 (14.1)	21 (12.4)	32 (13.0)
Radiotherapy			
Completed	10 (12.8)	52 (30.8)	62 (25.1)
Partial	5 (6.4)	9 (5.3)	14 (5.7)
No details	4 (5.1)	4 (2.4)	8 (3.2)
Surgery + Radiotherapy			
Completed	2 (2.6)	8 (4.7)	10 (4.0)
Incomplete	0	4 (2.4)	4 (1.6)
No treatment & treatment details not known	46 (60.0)	71 (42.0)	117 (47.4)

range reported from developing countries, the USA in the 1960s (Sankaranarayanan *et al.*, 1996). and Europe (Berrino *et al.*, 1995).

Our results have important implications for cervical cancer control in the developing world. Our studies, as well as the experience in Sweden in the precytology era (Pontén *et al.*, 1995), indicate that a programme of health education motivating women to seek early diagnosis and treatment and improving opportunities for early diagnosis and therapy can lead to improved survival outcome from cervical cancer.

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