

Cancer incidence, prevalence and survival in an aging Norwegian population

Astri Syse¹, Marijke Veenstra¹, Bjarte Aagnes² and Steinar Tretli²

1) Norwegian Social Research (NOVA)

2) Cancer Registry of Norway

Correspondence: Astri Syse, NOVA, Postboks 3223 Elisenberg, NO-0208 Oslo, Norway

E-mail: astri.syse@nova.no Telephone: +47 47032304

ABSTRACT

Background: Cancer is a disease closely associated with aging. Aging populations will thus lead to a pronounced increase in the absolute number of elderly persons with cancer, resulting in profound public health challenges in the coming decades. Older patients have distinct treatment and care needs, but are nevertheless largely overlooked in studies. We therefore examine cancer incidence, prevalence and survival among older cancer patients to help guide various stakeholders in the acute and more long-term handling of this patient group.

Data and methods: >400 000 cancers diagnosed in individuals age 65+ in 1975-2009 were extracted from the Cancer Registry of Norway. Descriptive analyses of incidence and prevalence were undertaken, and survival analysis was used to model survival.

Results: The absolute number of elderly (65-79 years) and oldest old (80+ years) patients has more than doubled since 1975, and will continue to grow towards 2030. A more than threefold increase in patients 80+ years has taken place. The largest patients groups comprise colorectal, prostate, lung and breast cancer. For all patients 65 and older, the median survival has increased with 135%. The increase has been most pronounced for the elderly patients. Surgical resection rates decline with increasing patient age. The difference in relative survival is around 8 percentage points at three years (60% vs 52%). It has been constant over time.

Conclusion: "Best practice" guidelines for the large and increasing group of older cancer patients remain to be established. The gain in length of lives must be balanced against patients' quality of life, and considered in a cost-benefit perspective for society at large.

BACKGROUND

Cancer is a disease strongly associated with aging, and the median age at diagnosis is close to 70 years in Norway (1). The increase in the number of elderly persons (2) together with stable and/or increasing cancer incidence rates (1,3,4) will result in a pronounced increase in the absolute number of elderly persons with cancer and thus in need of treatment and long-term follow-up and care (5,6). This will lead to significant public health challenges in the coming decades at a societal level in terms of the associated economic and non-economic costs and at an individual level in terms of treatment and care needs.

The vast majority of clinical trials have stringent eligibility criteria for trial entry (7,8), resulting in scarce inclusion of older patients. This has led to an inadequate understanding of appropriate treatment protocols for surgery, radiation and chemotherapy for older cancer patients, increasing with increasing patient age. It has further restricted the accessible knowledge of expected outcomes like for instance surgery-related complications and survival rates (9). Also patient-reported outcomes such as fatigue, pain, nausea and quality of life are largely lacking for older patients (10). Relative to younger patients, older patients are on average less fit and have a greater number of other illnesses which may interfere with cancer treatment

directly or indirectly (6,11-14), confirmed by a recent review by Marengoni et al (15). Older cancer patients are more costly than younger patients as they require longer hospital stays and experience a higher number of treatment-related complications (11,13,16-19). Older patients thus have distinctive needs in terms of diagnosis, treatment and care, but are nevertheless largely overlooked or excluded from studies due to challenges related to competing mortality or comorbidity (5,7, 13,14).

Some exceptions exist, however, and interest in geriatric oncology is emerging as population aging warrants more detailed knowledge of benefits and costs associated with treatment and care of older cancer patients (13,17). A recent review underscores for instance the need to carefully consider who should be aggressively treated among those of high age due to the residual high risk of adverse outcomes (20). This is underscored by a Norwegian study from 2011 which shows that the use of a comprehensive geriatric assessment may be useful in predicting both short- and longer-term outcomes of surgery in the oldest old patients (21). A retrospective study of all nonagenarian patients treated in a US hospital over the last two decades found that although 88% of patients were given active treatment, the rate of treatment-related mortality was very low (22). On the other hand, the mean survival of treated patients was 1.7 years, down to around

one year for advanced disease and up to barely two years for localized disease (ibid). Questions of treatment benefits versus costs, both economic and non-economic, thus remain.

Also in registry-based research, there is a limited focus on the oldest patients. Commonly reported five-year relative survival may be of limited use for patients 80 years and older who have short remaining life expectancies. Short-term measures such as one- and three-year survival have been suggested to be more relevant, but are rarely published. Our aims are therefore to utilize high quality data from the Cancer Registry of Norway to provide an updated overview of time trends in incidence, prevalence, short- and longer-term all-cause and relative survival among the elderly and oldest old cancer patients in Norway. A secondary aim is to identify characteristics associated with survival that may be relevant for patients, health care personnel, care plans and clinical guidelines in the acute and more long-term disease management, which have become particularly relevant in light of the recently implemented Coordination reform (23).

DATA AND METHODS

Data

Data on all Norwegian cancer cases diagnosed at 65+ years in the period 1975-2009 were obtained from the Cancer Registry of Norway (CRN). Mandatory reporting from clinicians, pathologists, and death certificates from 1953 onwards ensures completeness and high quality data (24). The CRN is linked to the Central Population Registry which provides vital statistics on all cancer patients. It is also matched regularly to the Norwegian Patient Registry for additional quality assurance. The overall completeness for all age groups combined was estimated to be 99% for the period 2001-2005 (ibid). During this time, 94% of the cases were morphologically verified (site-specific range 60-100%). Hematological malignancies (C90-95) and tumors of the central nervous system (C70-72) were most frequently underreported. The proportion of cancer cases with unknown primary site and records based on death certificate only (DCO) increases with increasing patient age (ibid). The accuracy and completeness of information on diagnosis (e.g. stage) and treatment (e.g. resection status) is thus likely falling with increasing patient age.

The method of diagnosis was defined as *clinical*, by *imaging or biochemical analysis, histological verification, death certificate only (DCO) or autopsy and unknown*. We defined surgery within the first course of treatment either as *no surgery* (including biopsy for diagnosis but not treatment), minor excisions or other resections with non-curative intents as *non-curative surgery*, major excisions with attempts at tumor removal as *curative surgery or unknown*, the latter including categories where surgery type is unknown but also those where it is unknown whether surgery actually

was performed. Stage was defined as *local, regional spread, distant spread*, and *unknown*, the latter category also comprising cases where staging is not applicable. Cancers were grouped based on topography using the International Classification of Diseases, version 10 (ICD-10) (25). The categories were *colorectal* (C15-C20), *prostate* (C61), *lung* (C34), *renal/bladder* (C64-C68), *female breast* (C50), *skin* (C43-C44, basal cell carcinomas exempted), *hematopoietic/lymphoid* (C81-C96), *female gynecological* (C51-C57), *pancreatic* (C25) and *other cancers*. The cancers were categorized as being either a *first* or *subsequent* primary cancer. Information on radiation, chemotherapeutic and hormonal treatment was largely missing and could not be reliably analyzed.

All cancers (N=443 545) diagnosed in individuals age 65 and above (N=398 072) in 1975-2009 were included in the descriptive analyses of incidence. As some persons are diagnosed with more than one cancer form after age 65, there is not a one-to-one relationship between the number of cancer cases and cancer patients. Site-specific analyses were undertaken for the largest groups; Colorectal, prostate, lung, renal, bladder, skin and breast cancer. These groups receive different treatments and have vastly varying outcomes in part due to the natural courses of the diseases but also due to variations in available treatment options.

Survival analyses were restricted to patients diagnosed with a first cancer at age 65 or above in 1975-2009 with a survival time greater than zero, excluding all cases diagnosed by death certificate only (DCO) or at autopsy (N=349 683). All patients were followed from date of diagnosis to date of emigration, death or January 1 2012, whichever occurred first. Norwegian life tables by sex, one-year age group and one-year calendar period updated through 2009 were downloaded from the human mortality database website (26), and data for the years 2010 and 2011 were extrapolated from the year 2009.

Methods

Cancer incidence, prevalence, all-cause and relative survival (excess mortality) among the elderly (65-79 years) and oldest old (80+ years) patients in Norway were examined. Analyses were undertaken to assess differences in cancer characteristics, diagnosis and treatment between the time periods 1975-1979, 1990-1994 and 2005-2008. Further analyses were carried out to provide an overview of the current (2009) annual cancer incidence burden. Descriptive statistics were used to examine demographic and diagnostic features of patients diagnosed after age 65 in the period 1975-2009 alive January 1 2012 (N=66 754). The oldest old cancer survivors (N=41 114) were examined specifically. The future cancer burden in terms of new cases and survivorship was predicted next, applying current cancer incidence and survival rates on projected populations (2).

All-cause survival by age group and diagnostic pe-

Table 1. Age distribution of cancer cases diagnosed in individuals age 65 and over in 1975, 1992 and 2009.

	1975 (N=7758)		1992 (N=13 076)		2009 (N=17 270)	
Age at diagnosis	N		N	% change ^a	N	% change ^a
65-79 years	5634		8894	58	10 663	89
65-69	1681		2373	41	3456	106
70-74	2073		3375	63	3664	77
75-79	1880		3146	67	3543	88
80+ years	2124		4182	97	6607	211
80-84	1336		2485	86	3233	142
85-89	576		1258	118	2307	301
90-94	179		372	108	872	387
95+	33		67	103	195	491

^aPercentwise change from 1975.

Table 2. Descriptive statistics of incident cancers diagnosed annually (2009) in individuals 65 years and older.

	65-79 years	80+ years	Total	
	(N=10 663)	(N=6607)	N	%
Male	60.5	49.6	9667	56.0
Female	39.5	50.4	7603	44.0
Histologically verified	96.5	80.4	15519	89.9
Diagnostic imaging only	2.2	7.0	726	4.2
Clinical examination only	0.5	1.8	179	1.0
DCO or autopsy	0.8	10.6	840	4.9
Unknown	0.0	0.1	6	0.0
No surgery	42.9	42.5	7383	42.8
Non-curative surgery	0.9	1.2	179	1.0
Curative surgery	55.1	44.9	8790	50.9
Unknown	1.0	11.4	918	5.3
Localized	60.4	54.0	9973	57.7
Regional spread	26.8	23.0	4359	25.2
Distant spread	10.0	10.1	1736	10.1
Unknown spread	2.8	12.9	1202	7.0
Colorectal	18.4	21.6	3401	19.7
Prostate	20.7	11.5	2916	16.9
Lung	11.4	9.0	1800	10.4
Renal/bladder	8.0	8.5	1424	8.2
Breast	7.5	6.5	1226	7.1
Skin	9.5	15.9	2094	12.1
Hematopoietic/lymphoid	7.9	8.3	1394	8.1
Female gynecological	4.7	4.2	775	4.5
Pancreatic	2.4	3.6	506	2.9
Other/unknown	9.4	10.9	1734	10.0
First cancer	81.1	75.5	13604	78.8
Subsequent cancer	18.9	24.5	3666	21.2

riod was estimated using the Kaplan-Meier estimator. Relative survival (RS) for all cancer sites combined and for selected subsites was estimated by life table methods (27). RS is the ratio of the observed survival proportion to the expected survival proportion derived from national life tables. Flexible parametric RS models estimating excess mortality ratios (EMR) were applied to assess differences in net cancer survival related to age and diagnostic period, and to examine the impact of potentially influential covariates (28,29). Covariates relating to patient, tumor, diagnostic work-up and treatment were added in this order, and model selection was guided by minimizing the Bayesian Information Criterion (BIC) (30). Three time periods were considered: 1975-1989, 1990-1999 and ≥ 2000 .

All analyses were undertaken in Stata 12, and the programs *strs* and *stpm2* were used for life table and survival modeling, respectively. The statistical significance level was set at 5%.

RESULTS

Cancer incidence

Changes in the age distributions of elderly and oldest old cancer patients from 1975 to 2009 are shown in Table 1. Patients were older and more numerous in 2009 compared to 1975 and more than 17 000 patients 65 years and older are diagnosed with cancer on an annual basis today. The absolute number of elderly (65-79 years) and oldest old (80+ years) patients has more than doubled since 1975. The increase has been largest in the oldest old group, where a more than threefold increase has taken place. Table 2 provides an overview of the characteristics of the oldest old patients diagnosed on an annual basis today.

The median age at diagnosis was 76 years for all cancer cases diagnosed after age 65 during the time period 1975-2009 (standard deviation (SD) 7 years). It has been fairly stable from 1975 to 2009. During the entire time span 1975-2009, the proportion of cancers histologically verified was 84% overall, whereas 5% were diagnosed by imaging only. A total of 8% were confirmed only via death certificates (DCO) or autopsy. The percentage histologically verified declined sharply with age (88% for age 65-79 vs 77% for 80+), whereas the DCO and autopsy proportion increased (7% for age 65-79 vs 10% for 80+). More men than women were diagnosed with cancer between age 65 and 79 (58% vs 42%), whereas the gender distribution was fairly equal after age 80. Overall, 85% were first cancers, but the proportion declined with increasing patient age (87% for age 65-79 vs 83% for 80+). Curative surgery was performed on around half of all cancer cases, but it was lower for the patients age 80+ relative to those 65-79 (45% vs 53%). The cancer report did not state whether or not surgery was performed in 8% of the cases, and this was related to age (6% for age 65-79 vs 11% for 80+).

Table 3. Descriptive statistics of incident cancer cases in 1975-79, 1990-1994 and 2005-09.

	1975-1979 (N=41 823)		1990-1994 (N=64 910)		2005-2009 (N=83 557)	
	65-79 years	80+ years	65-79 years	80+ years	65-70 years	80+ years
	N=29 093	N=12 730	N=43 926	N=20 984	N=48 075	N=35 482
	%	%	%	%	%	%
Male	56.7	52.3	58.2	50.4	60.0	50.3
Female	43.3	47.7	41.8	49.6	40.0	49.7
Histologically verified	76.8	66.0	88.5	78.3	95.4	80.9
Diagnostic imaging only	3.4	6.3	2.9	6.9	2.9	8.6
Clinical examination only	4.3	10.5	1.0	3.7	0.6	2.5
DCO or autopsy	15.5	17.3	7.6	11.1	1.0	8.0
Localized	54.1	54.2	56.0	55.3	46.2	39.6
Regional spread	15.3	12.8	21.3	16.3	25.5	23.3
Distant spread	27.3	23.6	15.0	13.3	11.5	11.4
Unknown spread	3.4	9.4	7.7	15.1	16.8	25.8
Colorectal	23.9	28.1	22.1	24.5	18.4	21.8
Prostate	14.2	16.2	15.1	15.8	20.7	12.8
Lung	8.4	3.8	10.8	5.2	11.5	8.5
Renal/bladder+A43	8.9	7.4	9.7	8.2	8.3	8.2
Breast cancer	9.0	7.8	8.0	8.5	7.3	6.8
Skin cancer	3.8	6.4	7.4	10.6	9.1	14.9
Hematopoietic/lymphoid	7.4	7.3	6.6	6.7	7.6	8.0
Female gynecological	6.3	4.3	5.4	4.5	4.7	4.3
Pancreatic	4.1	3.7	3.3	3.9	2.5	3.7
Other/unknown	14.0	15.0	11.6	12.1	9.8	11.0
First cancer	93.6	92.5	86.8	84.9	82.0	76.1
Subsequent cancer	6.4	7.5	13.2	15.1	18.0	23.9
No surgery	40.1	48.2	25.7	23.9	42.9	43.8
Non-curative surgery	5.7	6.3	11.7	16.3	1.3	1.7
Curative surgery	53.1	42.5	57.1	48.4	55.1	46.4
Unknown	1.1	3.0	5.5	11.4	0.7	8.2

A detailed description of cancer incidence for patients age 65 and above at diagnosis for an early, middle and late time period (1975-79, 1990-94 and 2005-09, respectively) is shown in Table 3. Overall, there has been an increase in the proportion of oldest old cancer cases that are histologically verified (from 66% to 81%), and a similar reduction in the proportion diagnosed based on DCO or autopsy (from 17% to 8%), but the trend is not very different from that observed for those 65-79 years old. The proportions diagnosed in local stages were fairly similar for the elderly and oldest old patients in earlier time periods. It has declined for all patients in the latest time period, but more so for the oldest old than the elderly (40% versus 46%), which may be attributed to an increased use of more advanced diagnostic equipment and tests. Due to changes in the coding practices at CRN, the proportion of patients with an unknown stage at diagnosis has risen sharply from the earliest time period to the latest time period. The pattern of change is, however, not very different for the elderly and the oldest old patients. The most common malignancies diagnosed in the oldest old today are colorectal (22%), skin (15%), prostate (13%), lung (9%) and renal/bladder (8%), and the distribution is not very different from that observed among elderly patients. The proportion of subsequent cancers is higher in the oldest old than in the elderly for all time periods, and it has increased over time (from 8% in the earliest time period to 24% today) with important implications for treatment and

cancer care. The oldest old patients receive curative surgery less often than younger cancer patients, with likely survival implications, but the difference has been relatively stable, around 10 percentage points, over time.

The age-specific incidence rates have been fairly stable for the high age groups over the last decade (1,3), with the exception of breast and prostate cancer where the uptake of screening is evolving also at higher ages (31,32). When we apply the current incidence rates to Statistics Norway's *high life expectancy* projected population 80 years and above for 2020, 2030 and 2040 (2), we find that the annual number of oldest old patients will increase only slightly up until 2020, whereas this age group will grow very fast from this point onwards. Up until 2030, the number of cancer cases diagnosed at age 80 or above will increase by about 70%, resulting in around 11 450 cancer diagnoses annually. Likewise, the increase up until 2040 will be around 140%, resulting in 15 700 cancer diagnoses annually in this age group.

Cancer prevalence

Concurrent with an increasing number of individuals being diagnosed with cancer in older ages, survival has increased over time for both younger and older patients. Cancer survivorship has thus become an issue also in relatively high ages. As can be seen from Table 4, in 2011 more than 41 000 of the oldest old persons were living with a 2-year history of cancer diagnosed

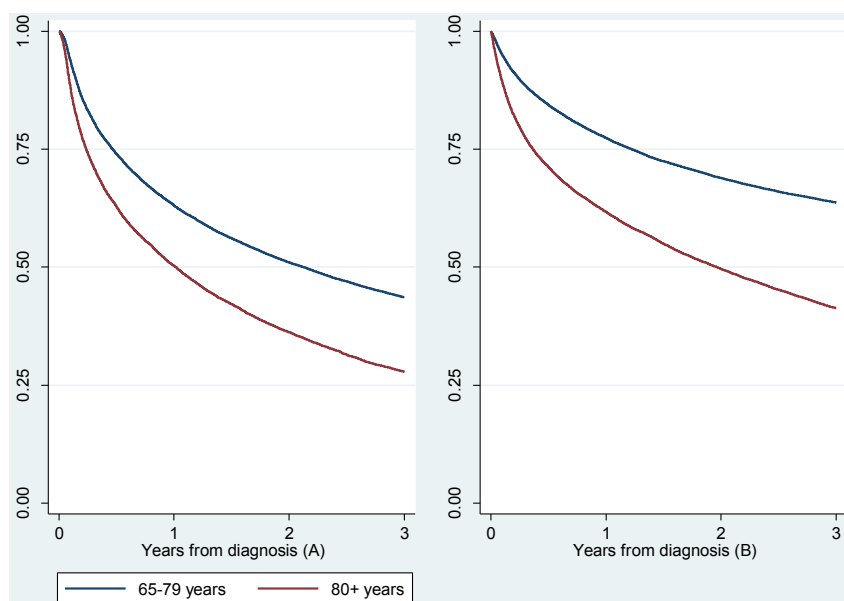


Figure 1. All-cause three-year survival by age below or above 80 at diagnosis, for patients diagnosed in 1975-79 (A) vs 2005-08 (B). Patients diagnosed in 2009 were not included as they had a maximum follow-up time of only two years.

Table 4. Descriptive statistics of cancer survivors 80 years and older per January 2012, alive for minimum 2 years post-diagnosis (N=41 114).^a

	Cancer survivors	
	N	%
Male	19780	48.1
Female	21334	51.9
Diagnostic year 1975-89	923	2.2
Diagnostic year 1990-99	10573	25.7
Diagnostic year 2000-09	29618	72.0
65-74 years at diagnosis	15424	37.5
75-84 years at diagnosis	21405	52.1
85+ years at diagnosis	4285	10.4
Histologically verified	40254	97.9
Diagnostic imaging only	730	1.8
Clinical examination only	116	0.3
Unknown	14	0.0
No surgery	9672	23.5
Non-curative surgery	162	0.4
Curative surgery	30910	75.2
Unknown resection status	370	0.9
Colorectal cancer	8886	21.6
Prostate cancer	7736	18.8
Skin cancer	7362	17.9
Breast cancer	5323	12.9
Renal/bladder cancer	4021	9.8
Female gynecological cancer	2420	5.9
Hematopoietic/lymphoid cancer	2021	4.9
Lung cancer	564	1.4
Pancreatic cancer	52	0.1
Other/unknown cancer	2729	6.6
First cancer	36360	88.4
Subsequent cancer	4754	11.6
Localized	24253	59.0
Regional spread	7333	17.8
Distant spread	737	1.8
Unknown spread	8791	21.4

^aLimited to individuals diagnosed at age 65 or above in the period 1975-2009.

in the period 1975-2009 after age 65, and the oldest person was 111 years old. The actual number of cancer survivors above 80 years of age is higher, as those recently diagnosed (i.e. during 2010 and 2011) could not be included due to data limitations. For the same reason, long-time survivors diagnosed before age 65 and/or before 1975 could not be included. Cancer survivors diagnosed in the period 1975-89 comprise, however, only 2% of the group and the latter exclusion is thus likely to matter very little.

Colorectal, prostate and breast cancer survivors are most prevalent in the population, and more than 97% had a histologically verified cancer. The majority of the 2-year survivors were between 75 and 84 years old at diagnosis (52%), and more than 75% had received curative surgery.

When we apply the current age-specific incidence rates and the current survival rates to the aforementioned future predicted populations, the estimated number of cancers diagnosed in individuals 80 years and older will be around 71 000 in 2030 and nearly 100 000 in 2040.

All-cause survival (Observed mortality)

Altogether, we observed 337 524 deaths of any cause during the maximum 36 year follow-up period (85%). A total of 222 151 persons died within three years (56%). All-cause three-year survival decreases substantially with increasing age, but has improved considerably from 1975-79 to 2005-08 (Figure 1). The median survival time for elderly patients diagnosed in 1975-79 was 2.1 years (95% confidence interval (CI) 2.0-2.2), 3.2 years (CI 3.1-3.3) in 1990-94, whereas it could not be calculated for those diagnosed in 2005-08. For the oldest old patients, the corresponding survival times were 1.0 (CI 1.0-1.1), 1.4 (CI 1.3-1.4) and 2.0 years

Table 5. Life table relative survival estimates (%) with 95% confidence intervals for all cancers and selected cancer forms by age at diagnosis and diagnostic period.^a

	65-79 years			80+ years		
	1-year	3-year	5-year	1-year	3-year	5-year
All cancers^b	73 (72-73)	60 (59-60)	54 (54-54)	64 (64-64)	52 (52-53)	47 (47-48)
1975-79	66 (65-66)	50 (49-51)	44 (43-44)	58 (57-59)	43 (42-45)	38 (37-40)
1990-94	72 (71-72)	58 (57-58)	52 (51-53)	64 (63-65)	51 (50-53)	45 (44-47)
2005-08	79 (79-80)	69 (69-70)	65 (64-65)	69 (68-70)	59 (58-60)	55 (54-56)
Colorectal cancer^b	69 (68-69)	53 (52-53)	47 (47-48)	58 (57-58)	45 (44-46)	42 (41-43)
1975-79	56 (55-58)	39 (38-41)	35 (33-36)	45 (43-47)	29 (27-31)	25 (23-28)
1990-94	68 (67-69)	53 (51-54)	47 (46-49)	56 (54-58)	42 (40-44)	39 (37-41)
2005-08	77 (76-78)	64 (62-65)	58 (57-60)	66 (64-67)	55 (53-57)	53 (50-56)
Prostate cancer^b	95 (94-95)	85 (85-86)	76 (76-77)	89 (89-90)	74 (73-75)	62 (61-63)
1975-79	90 (89-91)	71 (69-73)	59 (56-61)	81 (78-83)	61 (57-64)	50 (45-54)
1990-94	94 (94-95)	80 (79-81)	69 (68-71)	87 (85-89)	71 (68-74)	56 (52-60)
2005-08	99 (99-100)	96 (96-97)	94 (92-95)	94 (92-96)	85 (82-88)	77 (73-81)
Lung cancer^b	34 (33-35)	14 (13-15)	10 (9-10)	23 (22-24)	7 (6-8)	4 (3-5)
1975-79	32 (30-35)	10 (9-12)	7 (6-9)	22 (17-28)	6 (3-11)	4 (1-8)
1990-94	32 (30-34)	13 (12-14)	9 (8-10)	20 (16-23)	5 (4-8)	3 (2-6)
2005-08	39 (37-40)	18 (17-19)	13 (12-15)	25 (23-28)	8 (7-10)	4 (3-6)
Renal/bladder cancer^b	83 (82-84)	71 (70-72)	65 (64-66)	71 (70-72)	60 (58-62)	55 (53-57)
1975-79	79 (77-81)	64 (62-67)	57 (55-59)	66 (61-70)	53 (47-58)	47 (41-54)
1990-94	83 (81-84)	71 (70-73)	65 (63-67)	72 (69-75)	60 (56-65)	54 (49-59)
2005-08	86 (84-87)	76 (74-78)	72 (69-74)	76 (74-79)	68 (64-71)	65 (60-70)
Skin cancer^b	97 (97-97)	92 (92-93)	89 (88-90)	97 (96-97)	90 (89-91)	88 (86-90)
1975-79	96 (94-98)	90 (87-92)	84 (80-88)	94 (90-97)	87 (81-93)	87 (78-95)
1990-94	97 (95-98)	92 (90-94)	90 (88-92)	98 (96-99)	92 (89-96)	89 (83-94)
2005-08	98 (97-99)	94 (93-96)	91 (89-93)	98 (96-99)	95 (92-97)	91 (87-95)
Female breast cancer^b	96 (95-96)	87 (86-88)	81 (80-82)	91 (90-92)	81 (80-83)	74 (72-76)
1975-79	93 (92-94)	80 (78-82)	71 (69-74)	88 (85-91)	75 (70-80)	67 (61-74)
1990-94	95 (94-96)	87 (86-89)	80 (78-82)	91 (88-93)	80 (76-83)	72 (68-77)
2005-08	97 (96-98)	92 (90-93)	89 (87-90)	93 (91-95)	83 (80-86)	81 (76-86)

^aAll primary incident cases with a survival time > 0 were used in the estimations and a cohort approach was applied, except for in the overall calculations and in 5-year calculations for the latest time period where a complete approach was used due to incomplete follow-up time on those latest diagnosed. ^bAll primary incident cases diagnosed in the period 1975 to 2009 were used in the estimations.

(CI 1.9-2.2), respectively. For all patients 65 and older, the median survival has increased from 1.7 years (CI 1.6-1.7) in 1975-79 to 4.0 (CI 3.9-4.0) years in 2005-08, corresponding to a 135% increase.

Relative survival (Excess mortality)

Life table estimates are portrayed in Table 5 and show that age is an important prognostic factor. Although survival has increased over time, the difference between the elderly and the oldest old has been fairly constant over time: The three-year RS difference for all cancer forms combined was 16% for the earliest (50% vs 43%) and the latest (69% vs 59%) time period when comparing those 65-79 years old with those 80+. The mortality selection was most pronounced during the first year, and appeared to decline more gradually from this point onwards. RS was fairly good after skin, prostate and breast cancer, whereas it was very poor after lung cancer, for all age groups. The largest percent wise difference in three-year RS between the age groups was observed for lung cancer (18% vs 8%), whereas no age difference was observed for skin cancer (94% vs 95%). For colorectal, prostate, breast, renal and bladder cancer, the differences were 16%, 13%, 11% and 12%, respectively.

We observe improvements in RS from 1975 to today for many of the prevalent cancer forms, for both elderly and oldest old patients. For the latter group, the three-year RS changes have been most pronounced for colorectal cancer (from 29% to 55%), prostate cancer (from 61% to 85%) and for renal and bladder cancer (from 53% to 68%). There has been virtually no change in the RS after lung cancer, and the improvements after skin and breast cancer have been minor.

Excess mortality ratios from RS models are shown in Table 6. According to model C, survival was 32% worse for the oldest old patients compared to the elderly, and it was also 11% worse for men compared to women. Compared to those diagnosed in the 1970s and 1980s, a 19% increase in survival was observed for patients diagnosed during the last decade. No improvement was, however, observed for the patients diagnosed in the 1990s. Cancer form was included primarily as a control variable, and the results were in line with what is previously known. Also the effects of stage were as predicted, with two- to fourfold worse survival outcomes for more advanced stages. Survival is 37% better for patients with histologically verified cancers. Curative surgery is the factor most strongly associated with prolonged survival, and having recei-

Table 6. Excess mortality ratios from three relative survival models examining the influence of covariates on excess mortality.^a

	Model A		Model B		Model C	
	EMR ^b	95% CI ^c	EMR	95% CI	EMR	95% CI
Age at diagnosis						
65-79 years	1		1		1	
80+ years	1.42	1.40-1.44	1.39	1.37-1.41	1.32	1.30-1.34
Gender						
Female	1		1		1	
male	1.02	1.01-1.03	1.11	1.10-1.13	1.11	1.09-1.12
Year of diagnosis						
1975-89	1		1		1	
1990-99	0.84	0.83-0.85	0.94	0.93-0.96	1.03	1.02-1.05
≥ 2000	0.68	0.67-0.69	0.73	0.72-0.74	0.81	0.80-0.82
Cancer form						
Other/unknown			1		1	
Colorectal			0.68	0.67-0.69	1.02	0.99-1.04
Prostate			0.20	0.20-0.21	0.18	0.18-0.19
Lung			1.62	1.59-1.65	1.37	1.34-1.39
Renal/bladder			0.55	0.53-0.56	0.76	0.74-0.78
Breast			0.24	0.23-0.25	0.37	0.36-0.39
Skin			0.14	0.14-0.15	0.23	0.22-0.24
Hematopoietic/lymphoid			1.69	1.65-1.73	1.04	1.02-1.07
Female gynecological			0.50	0.49-0.52	0.65	0.65-0.67
Pancreatic cancer			2.00	1.95-2.05	1.83	1.78-1.87
Stage at diagnosis						
Localized			1		1	
Regional spread			2.36	2.32-2.41	2.27	2.23-2.31
Distant spread			6.04	5.95-6.15	4.40	4.33-4.47
Unknown spread			2.04	2.00-2.09	1.69	1.65-1.73
Diagnostic basis						
Not histologically verified ^d			1		1	
Histologically verified			0.45	0.45-0.46	0.63	0.62-0.64
Resection status						
No curative surgery ^d					1	
Curative surgery					0.27	0.27-0.28
Model diagnostics						
Log likelihood (model)	-570859		-498433		-485968	
BIC	1141871		997186		972294	
Degrees of freedom	12		25		28	

^aEstimates from flexible parametric models (Stata command:stpm2) with 5 degrees of freedom for main effects and 2 degrees of freedom for time-dependent effects. Spline parameters for the underlying hazard are not shown (available upon request). Age at diagnosis (all models) and resection status (model C) were modeled as time-dependent effects and were statistically significant at the p<0.01 level (not shown, available upon request). The final model is shown to the far right. ^bExcess mortality ratio. ^cConfidence interval. ^dIncludes also those with missing status.

ved curative surgery improved survival by around 70%. Due to the relatively good prognosis of skin cancer, the models in Table 6 were also set up excluding all skin cancer cases. The results remained, however, virtually identical. Models were also run excluding cancer form, but also here the results remained quite similar (available upon request).

Analyses stratified on the six most common cancer forms are shown in Table 7. The excess mortality associated with being 80 years and older was most pronounced for prostate cancer (52%), followed by renal and bladder cancer (35%) and lung cancer (30%). The effect of old age was least manifest for breast cancer (20%). Women had a 9% survival disadvantage after renal and bladder cancer relative to men, whereas the excess mortality for men was 48% for skin, 16% for colorectal and 12% for lung cancer. An improvement in survival from the earliest time period to the 1990s was observed only for breast and prostate cancer

(EMR 0.80 and 0.82, respectively). Improvement to the latest time period was observed for all cancer forms, skin and lung exempted. The improvement was greatest for prostate cancer, followed by breast, renal and bladder, and colorectal cancers. Curative surgery was the strongest predictor for survival after lung, colorectal and breast cancer.

Table 8 shows excess mortality ratios separately for elderly and oldest old patients. In general, the importance of most covariates appeared to be fairly similar across the two groups. Curative surgery was the strongest predictor for excess mortality in all age groups, but somewhat more important for the oldest old (EMR 0.22 vs 0.30). The improvement in survival from the earliest to the latest time period was, however, somewhat more pronounced for the elderly compared to the oldest old (EMR 0.78 vs 0.88). Cancers with distant spread resulted in worse outcomes for the elderly compared to the oldest old (EMR 5.09 vs 3.22).

Table 7. Excess mortality ratios from relative survival models stratified on common cancer forms.^a

	Colorectal		Lung		Renal/bladder		Skin		Prostate		Breast	
	EMR ^b	95% CI ^c	EMR	95% CI	EMR	95% CI	EMR	95% CI	EMR	95% CI	EMR	95% CI
Age at diagnosis												
65-79 years	1		1		1		1		1		1	
80+ years	1.28	1.25-1.32	1.30	1.25-1.35	1.35	1.27-1.43	1.26	1.09-1.46	1.52	1.45-1.60	1.20	1.11-1.30
Gender												
Female	1		1		1		1		N/A		N/A	
male	1.16	1.13-1.18	1.12	1.09-1.15	0.91	0.87-0.95	1.48	1.32-1.66				
Year of diagnosis												
1975-89	1		1		1		1		1		1	
1990-99	1.13	1.09-1.16	1.12	1.08-1.16	1.04	0.99-1.10	1.08	0.93-1.25	0.82	0.79-0.86	0.80	0.74-0.86
≥ 2000	0.87	0.85-0.89	0.99	0.96-1.02	0.84	0.79-0.89	1.03	0.89-1.19	0.42	0.39-0.44	0.71	0.66-0.77
Stage at diagnosis												
Localized	1		1		1		1		1		1	
Regional spread	2.24	2.18-2.31	1.40	1.35-1.45	4.48	4.22-4.76	13.13	11.13-15.47	2.26	2.06-2.48	3.02	2.77-3.30
Distant spread	3.89	3.76-4.03	2.46	2.37-2.55	8.07	7.57-8.62	26.58	22.67-31.15	5.71	5.43-6.01	8.54	7.82-9.32
Unknown spread	1.71	1.64-1.79	1.20	1.14-1.26	1.90	1.77-2.05	1.12	0.89-1.41	1.21	1.12-1.30	1.68	1.54-1.84
Diagnostic basis												
Not histologically verified ^d	1		1		1		1		1		1	
Histologically verified	0.63	0.61-0.66	0.70	0.67-0.73	0.57	0.54-0.62	0.24	0.15-0.37	0.64	0.46-0.52	0.51	0.45-0.57
Resection status												
No curative surgery ^d	1		1		1		1		1		1	
Curative surgery	0.22	0.22-0.23	0.21	0.19-0.23	0.49	0.47-0.53	0.97	0.83-1.13	0.64	0.60-0.68	0.31	0.29-0.34

^aEstimates from stratified flexible parametric models (Stata command:stpm2) with 5 degrees of freedom for main effects and 2 degrees of freedom for time-dependent effects. Spline parameters for the underlying hazard are not shown (available upon request). Age at diagnosis and resection status were modeled as time-dependent effects and were statistically significant at the $p < 0.01$ level, age for breast and skin cancer excepted (not shown, available upon request). ^bExcess mortality ratio. ^cConfidence interval. ^dIncludes also those with missing status.

DISCUSSION

We have illustrated the pronounced changes that have taken place in incidence, prevalence and survival for the oldest old patients over the last thirty to forty years, and shown that these changes will become even more prominent over the next twenty to thirty years as population aging accelerates. An increase in the number of patients aged 80 and above from a little over 2000 in 1975 to around 16 000 in 2040 will necessarily draw resources, both economic and non-economic, from an already strained public health care sector. According to a recent report on future hospital needs in Norway, the expected increase in the number of persons 70+ will by year 2030 demand 1.5 million additional hospital days per year which amounts to almost 5000 additional hospital beds (33). This corresponds to a nearly 50% increase in the number of beds available nationally in 2009, roughly six to seven hospitals the size of the Ullevaal division of Oslo University Hospital in Norway (ibid). Likewise will the future handling of more than 100 000 cancer survivors 80 years and older require a restructuring of services. The latter estimate is likely a gross underestimate, as the survival rates have improved markedly over the last decades and are likely to continue improving in the near future. The recently implemented Coordination reform focuses on health care organization in aging populations and attempts to minimize costs by moving a larger part of services from specialist to primary care (23), but will necessitate vaster resources directed also to the primary care sector.

Consensus recommendations and national guidelines have traditionally primarily focused on younger patients due to the lack of clinical data on treatment benefits as well as adverse effects in the oldest old patient groups. With the current population aging, the attention is to a larger extent expanded to include the oldest old patients. A revised national cancer strategy will be released towards the end of 2012 focusing on capacity, quality and organization of treatment and care to help ensure that future challenges will be met in a comprehensive manner (34), hopefully diverting attention also to the oldest old patients in terms of the proposed focus on transitions of services between different care levels and long-term effects. The proposed time perspective is, however, relatively short as the main focus is directed to the years 2013-2017 (ibid). In terms of personnel, equipment, and appropriate facilities such as nursing homes and community living units, such a short time perspective may be insufficient. Similarly, the observed increase in survival documented also for the oldest old patients will have implications for long-term survivorship follow-up of individuals in their 80s, 90s and 100s. As adverse short-term and long-term effects of the disease itself as well as treatment are more prevalent at older ages, this will need to be taken into consideration in future cancer strategies and plans.

Diagnosis and treatment of elderly and oldest old patients

Due to improvements in early diagnosis and screening, particularly for prostate and breast cancer (32,35), some of the improvement in survival observed over time

Table 8. Excess mortality ratios from relative survival models stratified on age at diagnosis.^a

	65-79 years		80 years and older	
	EMR ^b	95% CI ^c	EMR	95% CI
Gender				
Female	1		1	
Male	1.11	1.10-1.13	1.09	1.07-1.11
Year of diagnosis				
1975-89	1		1	
1990-99	1.02	1.01-1.04	1.05	1.02-1.07
≥ 2000	0.78	0.77-0.79	0.88	0.85-0.90
Cancer form				
Other/unknown	1		1	
Colorectal	0.97	0.95-0.99	1.08	1.05-1.11
Prostate	0.18	0.18-0.19	1.19	0.18-0.20
Lung	1.42	1.39-1.45	1.15	1.11-1.20
Renal/bladder	0.75	0.73-0.78	0.75	0.72-0.78
Breast	0.40	0.38-0.41	0.31	0.29-0.33
Skin cancer	0.25	0.23-0.26	0.18	0.15-0.20
Hematopoietic/lymphoid	1.05	1.02-1.09	1.03	0.99-1.07
Female gynecological	0.60	0.58-0.62	0.76	0.73-0.80
Pancreatic	1.96	1.90-2.02	1.53	1.47-1.60
Stage at diagnosis				
Localized	1		1	
Regional spread	2.46	2.41-2.51	1.96	1.90-2.02
Distant spread	5.09	4.99-5.20	3.22	3.12-3.32
Unknown spread	1.71	1.66-1.75	1.56	1.51-1.61
Diagnostic basis				
Not histologically verified ^d	1		1	
Histologically verified	0.60	0.59-0.62	0.65	0.63-0.66
Resection status				
No curative surgery ^d	1		1	
Curative surgery	0.30	0.29-0.31	0.22	0.22-0.23
Model diagnostics				
Log likelihood (model)	-361930		-123202	
BIC	723910		246696	
Degrees of freedom	25		25	

^aEstimates from flexible parametric models (Stata command:stpm2) stratified by age with 5 degrees of freedom for main effects and 2 degrees of freedom for the time-dependent effect. Spline parameters for the underlying hazard are not shown (available upon request). Resection status was modeled as a time-dependent effect and was statistically significant at the p<0.01 level (not shown, available upon request).

^bExcess mortality ratios. ^cConfidence interval. ^dIncludes also those with missing status.

might be a result of lead time bias, with individuals living longer with a known diagnosis but not necessarily having a real implication for the time of death. The degree to which screening continues to be used with increasing age and how screening during middle or older age affects survival in the oldest old remains, however, a topic for discussion (35,36), and it is not clear how to interpret the observed findings on the changes over time by age in the survival after breast and prostate cancer.

We found that the oldest old patients receive histological verification of their diagnosis to a lesser extent than older patients. In earlier days, this was often thought to be reflective of less aggressive treatment plans. With improvements in clinical imaging tools, patients with cancers which are not histologically verified may still be handled appropriately. This might be reflected also in this study as the effect of histological

verification is quite similar across age groups although the selection is much greater among the oldest old.

Today's complex cancer therapy regimens may be more difficult for the oldest old patients to follow, and health care interventions directed and adapted more specifically to this broad subgroup might be warranted (37,38). Surgery remains the primary mode of curative treatment for cancer but resection rates decrease with increasing patient age, as is observed also in this study. The main reason being increased risks of peri- and postoperative adverse events, which are consistently documented to be much more frequent in the oldest old patients (12,13), even though there is a strongly selected group of "fit" oldest old patients who receive surgery (22). Despite the strong selection, the oldest old are more expensive to treat overall compared to younger patients. This is mostly due to the average length of hospital stays being longer and the higher

number of admittances due to postoperative complications (15,18). In line with this, we observe the largest age differences in survival outcomes after lung cancer which are difficult to operate on, whereas there is hardly any difference after skin cancer requiring less extensive surgery. At the same time, there have been few improvements over time for these cancer forms, while rather large improvements for the oldest old have been seen after colorectal, prostate, renal and bladder cancer. Surprisingly, the modeled improvements in survival are only statistically significant for the latest time period. When stratifying on age above and below 80 years at diagnosis, we see that the effect of covariates tend to be very similar, although the change over time has been more pronounced for the elderly than the oldest old patients. Curative resection is a stronger predictor for advantageous survival among the oldest old, whereas advanced stage leads to worse consequences for the elderly compared to the oldest old patients. For the most prevalent cancer forms, we see that curative resection is particularly important for lung, colorectal and breast cancer. Skin cancer is less invasive and treatment is generally less aggressive. We thus expected lesser age differences between elderly and oldest old patients for this cancer form. Surprisingly, this was in general not observed. Neither did the overall estimates change when skin cancer was excluded from the analyses.

To summarize, relatively withstanding low curative surgery rates and pronounced complication rates in the oldest old cancer patients have resulted in a greater percent wise survival increase for the younger elderly patients. The optimal use of chemotherapy and radiation in a curative perspective is currently debated in older patients, and assessment scales, guidelines and protocols are slowly developing as evidence continues to emerge (38-42). As we only have information on surgery, benefits and risks associated with chemotherapy or radiation is not further discussed.

Methodological considerations, limitations and future research needs

The validity and completeness of data on the oldest old patients remains a problem both for research purposes and for the patients themselves as "good" treatment requires adequate diagnosis and treatment. Furthermore, the influence of competing causes of death, both in the registration procedures and as a methodological problem in the analyses arise in studying the impact of cancer in the elderly and oldest old (27). Competing causes of death analyses will need to complement our study to ensure adequate interpretations of studies that consider changes in cancer incidence and prognosis among the very old.

Norway is a supposedly egalitarian society with free public health available to all citizens, both young and old. At the same time, the public health care system attempts to minimize costs and thus demands fairly strict evidence for the implementation of newly avail-

able surgical or pharmaceutical treatment regimens (see e.g. <http://oncolex.no> for a list of available drugs in Norway), compared to for instance in the US where the reimbursement system promotes treatment of both very ill and very old patients (43). Norway nevertheless generally performs well in more general international comparisons of cancer survival, but these analyses are generally limited to individuals below age 75 (3,44). Detailed studies on outcomes cross-nationally after cancer in the oldest old are largely lacking.

At an individual level, knowledge of treatment options and expected outcomes are important for persons with cancer and their next of kin to ensure that they receive optimal treatment and care, and more so today than previously with greater demands of patients making informed choices in discussions with providers (45,46). Such information is also of utmost relevance for those who are responsible for, in a broad sense, aiding cancer patients. Whether or not the elderly and oldest old cancer patients are appropriately handled in the health care system or treated disadvantageously due to their high age is not obvious today. The lack of specific guidelines accounting for individual characteristics of patients, such as biological and physiological age, comorbidities, mental health status, prescription medication, social support and living situation, means that many medical decisions are made on an individual basis by individual health care providers or teams. Both *overtreatment* and *undertreatment* is likely to occur, with consequences for resource utilization in terms of for instance time and treatment costs at a societal level and adverse effects at an individual level in terms of reduced survival or multiple negative side-effects of cancer treatment. One solution could be to accumulate a knowledge base available to the larger medical community to draw experience from, which could aid clinicians in deciding *not* to treat patients due to poor outcome and/or high costs, and to adequately interpret findings from cancer studies concerned with quality and costs during diagnosis, treatment, and long-term follow-up. One recent suggestion entails utilizing measures of patients' likely remaining life expectancies to help clinicians and patients balance treatment burdens with expected gains in remaining length of lives (47).

CONCLUSION

We have provided an indication of the current cancer burden in the elderly and oldest old population in Norway, and shed light on the pronounced changes that have occurred over the last thirty to forty years. We have also presented coarse estimates of future changes that are likely to take place. Aging populations and stable or increasing cancer incidence and survival rates have resulted in a pronounced increase in the absolute number of elderly persons with (a history of) cancer in need of treatment and long-term follow-up and care, and this increase is expected to

continue, particularly strongly from 2030 onwards. This will in turn lead to profound public health challenges in the coming decades, as older patients and survivors have distinctive needs in dealing with adverse short-term and long-term effects of the disease itself as well as the treatment. Nevertheless, “best

practice” guidelines for specific age and comorbidity segments of the oldest old population remain to be established. Discussions relating to the balance between gains in lengths of lives and patients’ quality of life viewed in terms of a cost-benefit perspective for society at large will likely emerge.

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