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#### **ORIGINAL ARTICLE**

### Cancer survival in Lithuania after the restoration of independence: Rapid improvements, but persisting major gaps

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#### ABSTRACT

**Background.** Following restoration of political independence in 1990, Lithuania underwent rapid societal and economic changes. We aimed to assess trends in cancer survival in the first two decades following these changes.

**Material and methods.** We used population-based data from the Lithuanian Cancer Registry and period analysis techniques to examine trends in one-, 2–5- and five-year relative survival between 1995–1999 and 2005–2009 for 24 common cancers in Lithuania.

**Results.** Between 1995–1999 and 2005–2009, five-year relative survival increased significantly for 20 of 24 cancers, and for 10 cancers the increase exceeded 10% units. Five-year relative survival estimates reached 46%, 69% and 91% for colorectal, breast and prostate cancer in 2005–2009, respectively, while patients with testicular cancer, Hodgkin's or non-Hodgkin's lymphoma had a five-year relative survival of 77%, 75% and 50%, respectively.

**Conclusion.** We found a rapid increase in survival for most forms of common cancers in Lithuania between 1995 and 2009. Nevertheless, several cancers with effective therapies exhibit considerable gaps compared with Northern and Western European countries. Despite ongoing rises in survival, mortality declines are not yet manifesting for important common cancers such as breast and colorectal cancer. Rapid incidence rises suggest that increases in survival for prostate and thyroid cancers are massively influenced by early detection-related effects. Improving the availability of effective therapies, and carefully planned early detection programs may help to increase cancer survival in Lithuania in the future.

Population-based cancer survival is a most important outcome measure for cancer patients, and survival estimates also indicate the overall effectiveness of oncology care in a healthcare system. In Lithuania, after the restoration of independence in 1990, and the subsequent transition to open market economy, the healthcare system reforms led to the conversion of the inherited centralized system to an insurancebased healthcare system. The occurrence of cancer in the country, as well as the outcomes of oncologic care can be evaluated based on data from the Lithuanian Cancer Registry, which covers the entire population of the country [1]. While the registry has been contributing to international publications, such as the Cancer Incidence in Five Continents series [1] and also participated in the EUNICE survival cooperation [2–4], the availability of up-to-date survival information is still limited. Comprehensive analysis of long-term survival trends have not been reported from Lithuania before, and such analysis is also generally scarcely available from the Eastern part of Europe. In this study, we report up-to-date survival estimates for the 2005–2009 period, examine long-term trends in survival for 24 common cancers in Lithuania between 1995–1999 and 2005–2009 and interpret changes in survival considering additional information from incidence and mortality trends.

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#### Material and methods

#### Data sources

Incidence and follow-up data for this study were provided by population-based Lithuanian Cancer Registry which has been in operation since 1978. The registry covers the entire population of the country, which, mainly due to migration, decreased by around 12% in the last 10 years to around 3 million residents according to the 2011 census [5]. Data collection is based on mandatory notification of all cancer cases that come to the attention of all physicians, hospitals and other health institutions in the country. Additionally, death certificate information, and population registry information to verify vital status is available. In the current analysis, patients diagnosed with cancer between 1990 and 2009 were considered, excluding non-melanoma skin cancers, non-malignant neoplasms and childhood cancers (diagnosis at age < 15 years), as well as cancers registered by death certificates only (DCO) or autopsy only. Cancers were classified according to ICD-10, and the 24 most common cancers were determined according to the total number of incident cases between 1990 and 2009. This way, common gastrointestinal cancers (esophageal, stomach, liver, gallbladder, pancreatic and colorectal), hematological malignancies [Hodgkin's lymphoma (HL), non-Hodgkin's lymphoma (NHL), multiple myeloma and leukemia], urological cancers (kidneys, bladder, prostate and testicular), cancers of the female genital organs (cervix uteri, corpus uteri and ovarian) and the female breast, and other common cancers (thyroid gland, brain and nervous system, oral cavity, larynx, lung and melanoma of skin) were included in the analysis. Incidence data was available from the cancer registry, while National mortality data were available from Statistics Lithuania [6].

#### Survival analysis

We calculated one-year, conditional 2–5-year (denoted hereinafter as 5 | 1-year survival) and cumulative five-year survival estimates for the periods 1995– 1999, 2000–2004, and 2005–2009. Period survival analysis was used throughout as it provides more upto-date survival estimates than traditional cohortbased analysis [7]. Additionally, for the period of 2005–2009, TNM classification-based [8] stagespecific estimates were also calculated for colorectal, lung, and breast cancer. Relative survival estimates were derived as a ratio of the absolute survival of the cancer patients divided by the expected survival of an age- and gender-matched group of the underlying general population. Expected survival estimates were derived using the Ederer II method. Survival calculations were done with the Stata statistical package, using the freely available "strs" command [9], which was set up to allow for model based period analysis [10] to identify statistically significant changes in periodspecific relative survival over time.

#### Age adjustment

Age standardization for incidence and mortality trends, as well as survival estimates and standard errors was done using four age groups (15-44, 45-59, 60-74 and 75+) for all cancers with the exception of brain and nervous system cancer where the two oldest age groups were combined, also for prostate and testicular cancers, for which the age groups 15-59, 60-74, 75+ and 15-29, 30-44, 45+ were used, respectively. Adjustment was made using weights from International Cancer Survival Standards (ICSS) proposed by Corazziari et al. [11].

#### Results

Overall, 190 422 cancer cases with one of the 24 most common ICD-10 diagnoses were reported to the Lithuanian Cancer Registry between 1995 and 2009. After the exclusions, including 4.3% of patients reported by DCO only, 95.3% could be included into the analysis. Table I provides, for each examined period, the numbers of cancer cases by localization, the median age at diagnosis, the proportion of patients with a verified (by histology or cytology) diagnosis, and the proportionate change in number of cancer cases compared to the previous period. In 1995–1999, the most common cancers were lung, colorectal and breast cancer, while in 2005-2009, prostate cancer became the most common cancer, after case numbers have increased more than fourfold within a decade, followed by colorectal, breast, and lung cancer. Marked rises were also seen in the number of cases with thyroid gland and NHL, and also skin melanoma. At the same time an important decrease of newly diagnosed stomach and lung cancer cases was seen over the periods of the study. Median age at diagnosis increased among skin melanoma patients, and also for brain and nervous system cancer and NHL, while a large decrease (-4 years) was seen for prostate cancer patients. For many types of cancers, the proportion of diagnoses with morphological verification increased during the last decade – the largest increases in proportions were seen for pancreas, liver, prostate, kidney and stomach cancers.

Table II provides age-adjusted five-year relative survival estimates and their standard errors for each of the three examined periods (1995–1999, 2000– 2004 and 2005–2009) for 24 most common cancers in Lithuania, as well as the total change in survival

		1995–1999			2000-2004				2005–2009				
Site	ICD-10	N	MA	V (%)	Ν	MA	V (%)	Change (%)*	N	MA	V (%)	Change (%)*	
Oral cavity	C00-C14	1812	60	94.3	2028	61	94.0	+11.9	1820	60	93.1	-10.3	
Esophagus	C15	754	63	75.1	807	63	80.4	+7.0	820	62	81.5	+1.6	
Stomach	C16	5343	67	76.5	4997	68	82.9	-6.5	4240	69	86.6	-15.1	
Colorectal	C18-C21	6159	68	78.3	6975	69	84.6	+13.2	7065	70	86.7	+1.3	
Liver	C22	632	68	42.7	612	69	65.5	-3.2	640	70	65.0	+4.6	
Gallbladder	C23,C24	573	70	68.6	620	71	69.7	+8.2	470	73	73.0	-24.2	
Pancreas	C25	2010	68	41.6	2118	69	53.3	+5.4	2007	69	65.6	-5.2	
Larynx	C32	1032	60	92.8	991	61	92.8	-4.0	969	62	93.6	-2.2	
Lung	C33,C34	7868	65	66.6	7725	67	72.0	-1.8	6716	67	71.4	-13.1	
Skin melanoma	C43	987	58	97.1	1122	60	98.0	+13.7	1289	63	96.7	+14.9	
Breast (female)	C50	5740	59	90.2	6438	61	92.0	+12.2	7033	61	93.4	+9.2	
Cervix uteri	C53	2198	53	91.9	2489	51	91.1	+13.2	2416	51	93.6	-2.9	
Corpus uteri	C54	2176	62	95.4	2515	63	95.3	+15.6	2623	64	96.1	+4.3	
Ovary	C56	2055	62	84.7	2032	63	85.8	-1.1	1950	62	88.1	-4.0	
Prostate	C61	3493	72	76.4	7038	72	92.1	+101.5	15348	68	95.5	+118.1	
Testis	C62	159	33	95.6	187	35	97.9	+17.6	189	33	95.8	+ 1.1	
Kidney	C64	2398	64	66.3	2886	65	74.7	+20.4	3135	65	79.8	+8.6	
Bladder	C67	2013	69	78.8	2312	70	84.0	+14.9	1938	71	82.2	-16.2	
Brain and nervous system	C71,C72	1017	56	78.6	1083	58	83.4	+ 6.5	1153	61	83.3	+ 6.5	
Thyroid	C73	712	55	95.1	1316	54	96.8	+84.8	1767	54	99.1	+34.3	
Hodgkin's lymphoma	C81	490	33	100.0	376	35	100.0	-23.3	371	33	99.7	-1.3	
Non-Hodgkin's lymphoma	C82-C85	832	63	100.0	1290	65	99.3	+55.0	1547	68	99.3	+19.9	
Multiple myeloma	C90	526	67	100.0	696	67	99.4	+32.3	720	68	98.6	+3.4	
Leukemia	C91-C95	1927	66	99.6	1924	68	99.4	-0.2	1822	69	98.1	-5.3	

Table I. Number of cases (N), median age at diagnosis (MA), proportion of morphologically verified cases (V), and proportionate change in case numbers versus the preceding period, 24 most common cancers in Lithuania, 1995–1999 to 2005–2009.

\*Percent change in the number of cases compared to the previous period.

between 1995–1999 and 2005–2009, and the p-value obtained for the statistical significance of the change. The highest five-year relative survival in 2005–2009 was found for patients with thyroid and prostate cancer, whose relative survival slightly exceeded 90%. Five-year relative survival estimates were around 75% for patients with testicular and corpus uteri cancer, and also for HL, and slightly below 70% for skin melanoma and breast cancer. Relative survival remained between 50% and 40% for NHL, colorectal and larynx cancer, and leukemia. The lowest fiveyear relative survival (between 8% and 4%) was found for patients with lung, liver, esophageal and pancreatic cancer.

Between 1995–1999 and 2005–2009, the largest numerical increase in five-year relative survival was found, by far, for prostate (+47%), followed by increases between 20–10% units for thyroid and kidney cancer, HL, breast cancer, multiple myeloma, NHL, also testicular, colorectal, and larynx cancer. For cervical and corpus uteri cancer, leukemia, bladder, gallbladder, ovarian cancer, skin melanoma and liver cancer, survival rose by between 10% and 5% units – all of the aforementioned rises in survival were statistically highly significant. Finally, only increases below 5% units, or minor decreases, were seen in the five-year relative survival of patients with stomach, brain and nervous system, pancreas, lung, oral cavity and esophageal cancer.

Table III presents one-year and 5 1-year conditional survival between 1995-1999 and 2005-2009, as well as the change in the two survival measures between 1995-1999 and 2005-2009, and p-values obtained for the significance of the survival changes. With the exception of oral cavity, esophageal and larynx cancer, and HL, one-year survival increased statistically significantly, by 4-10% units for nine types of cancer, and by more than 10% units for 11 types of cancer. Consistent and statistically significant increases in both one-year and 5 1-year conditional survival were found for colorectal, breast, cervix, prostate, kidney and thyroid cancer, and for NHL, multiple myeloma and testicular cancer. However, a strong decline in 5 | 1-year conditional survival was seen for many cancers with dismal prognosis, such as pancreatic, lung, liver and brain and nervous system cancers.

Table IV presents information on the availability and distribution of stage for colorectal, lung and breast cancer, as well as age-adjusted stage-specific five-year relative survival estimates for 2005–2009. For colorectal cancer, survival decreased strongly with increasing disease spread, from 85% among those with localized disease to 69%, 49% and 6% for

Table II. Period survival estimates and changes in age-adjusted 5-year relative survival of common cancers in Lithuania between 1995–1999 and 2005–2009.

	1995–1999		2000-	-2004	2005-2009			
Site	PE	SE	PE	SE	PE	SE	Change <sup>4</sup>	p-value
Oral cavity	37.8	1.9	35.1	1.7	35.5	1.6	-2.3	0.054
Esophagus	7.9	1.4	4.0	0.7	5.2	1.0	-2.6	0.197
Stomach	18.0	0.6	19.3	0.6	21.6	0.7	+3.6	< 0.001
Colorectal	34.0	0.8	41.2	0.7	45.9	0.7	+12.0	< 0.001
Liver	2.4	0.6	5.4	0.9	7.4	1.2	+5.0	< 0.001
Gallbladder	9.5	1.3	10.7	1.6	16.8	2.0	+7.4	< 0.001
Pancreas	4.0	0.4	5.4	0.5	4.4	0.5	+0.4	< 0.001
Larynx	34.2	2.6	42.8	2.7	44.7	2.6	+10.5	< 0.001
Lung	8.3	0.4	8.0	0.3	7.9	0.4	-0.4	< 0.001
Skin melanoma	63.8	2.0	65.9	1.7	69.2	1.6	+5.4	0.001
Breast	53.0	1.1	63.2	0.9	69.0	0.9	+16.0	< 0.001
Cervix uteri	49.4	1.2	51.3	1.1	59.2	1.2	+9.7	< 0.001
Corpus uteri	66.4	1.7	70.3	1.4	75.1	1.3	+ 8.7	< 0.001
Ovary	25.2	1.2	29.0	1.0	32.0	1.1	+ 6.8	< 0.001
Prostate <sup>1</sup>	44.2	1.5	63.3	1.3	90.7	0.7	+46.6	< 0.001
Testis <sup>2</sup>	64.5	5.0	76.2	4.6	76.7	4.6	+12.2	< 0.001
Kidney	43.4	1.6	52.1	1.3	62.1	1.2	+ 18.7	< 0.001
Bladder	48.6	1.5	54.6	1.3	56.4	1.4	+7.8	< 0.001
Brain and nervous system <sup>3</sup>	17.7	1.3	19.0	1.1	20.6	1.2	+2.8	0.145
Thyroid	72.7	1.5	82.2	1.5	92.3	1.2	+19.7	< 0.001
Hodgkin's lymphoma	58.4	2.2	68.6	2.3	74.6	2.3	+16.2	< 0.001
Non-Hodgkin's lymphoma	35.0	2.3	39.1	1.8	49.5	1.5	+14.5	< 0.001
Multiple myeloma	19.5	1.9	20.5	1.9	34.9	2.2	+15.4	< 0.001
Leukemia	33.8	1.3	31.5	1.2	41.8	1.4	+8.0	< 0.001

PE, period estimate; SE, standard error.

 $^{1}$ 15–59, 60–74 and 75 + age groups were used for age adjustment;  $^{2}$ 15–29, 30–44, 45 + age groups were used for age adjustment;  $^{3}$ 15–44, 45–59 and 60 + age groups were used for age adjustment;  $^{4}$ Percent units change in survival between 1995–1999 and 2005–2009.

locally advanced, regional and metastatic disease, respectively. For lung cancer, patients with localized disease had a more favorable five-year survival of 37%, while for all other stages, survival estimates remained below 10%. Among breast cancer patients, 48% had localized disease with a 91% five-year survival probability. Less than 2% of patients had locally advanced disease, with a five-year survival of 62%, which was slightly lower than the estimate (65%) for the 42% of patients with regional disease. Those with a metastasis at diagnosis (9% of patients) had the lowest survival expectations (13%).

Supplementary Figures 1–5 (available online at http//informahealthcare.com/doi/abs/10.3109/ 0284186X.2014.888495) present age-adjusted incidence and mortality trends for the cancers analyzed in this study. Concurrent trends of incidence and mortality will be utilized for interpreting survival trends in the discussion.

#### Discussion

Our study provides the first population-based evaluation of long-term survival trends in Lithuania,

provides up-to-date long-term survival estimates for the 2005–2009 period, and a comprehensive interpretation of survival trends using accompanying information on cancer incidence and mortality trends. Importantly, we found statistically significant survival increases for 20 of 24 common cancers between 1995–1999 and 2005–2009. For large number of cancers with statistically significant survival rises, increases in survival were of clinically meaningful magnitude both for one-year and 5 | 1-year conditional survival, reassuringly suggesting that medical progress has been ongoing in the recent decade in the area of oncology in Lithuania. For 10 cancers, the overall increase was remarkably strong, exceeding 10% units.

Using additional incidence and mortality information (Supplementary Figures 1–5, available online at http//informahealthcare.com/doi/abs/10.3109/ 0284186X.2014.888495) for the interpretation of survival changes, it is necessary to note that the very large increases in prostate and thyroid cancer incidence, accompanied by no or little mortality decline suggest that increases in survival are explained by early detection and/or overdiagnosis effects rather

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Table III. Period survival estimates in age-adjusted 1-year and conditional 5 | 1-year relative survival of common cancers in Lithuania between 1995–1999 and 2005–2009.

	1995–1999		200	2000-2004		2005-2009		1-year		5   1-year	
Site	1-year	5   1-year	1-year	5   1-year	1-year	5   1-year	Change <sup>4</sup>	p-value	Change <sup>4</sup>	p-value	
Oral cavity	60.2	61.9	59.0	58.6	55.0	63.9	-5.2	0.034	+2.0	0.756	
Esophagus	22.1	34.6	17.0	23.2	20.2	26.1	-1.9	0.327	-8.5	0.379	
Stomach	32.6	55.5	35.4	54.0	40.2	53.9	+7.5	< 0.001	-1.5	0.462	
Colorectal	57.3	58.4	62.9	65.6	68.2	67.3	+10.9	< 0.001	+ 8.9	< 0.001	
Liver	5.7	45.5	11.6	45.0	20.3	36.6	+14.6	< 0.001	-8.9	0.828	
Gallbladder	18.5	47.9	23.9	44.1	32.9	47.2	+14.4	< 0.001	-0.7	0.766	
Pancreas	9.1	44.9	14.5	35.9	17.5	25.2	+8.4	< 0.001	-19.7	< 0.001	
Larynx	63.3	53.1	72.3	58.9	70.7	62.9	+7.4	0.099	+9.8	< 0.001	
Lung	21.2	39.7	22.5	35.0	26.4	28.0	+5.2	< 0.001	-11.7	< 0.001	
Skin melanoma	85.2	75.0	86.0	76.4	89.7	77.2	+4.5	0.001	+2.3	0.069	
Breast	82.3	64.0	85.2	74.4	90.0	76.6	+7.6	< 0.001	+12.5	< 0.001	
Cervix uteri	73.7	66.7	74.3	68.1	79.4	73.7	+5.7	< 0.001	+7.0	< 0.001	
Corpus uteri	80.6	81.0	85.5	81.6	89.2	83.8	+8.6	< 0.001	+2.8	0.413	
Ovary	47.8	52.4	54.1	53.4	60.1	51.1	+12.3	< 0.001	- 1.3	0.113	
Prostate <sup>1</sup>	74.6	59.3	86.8	72.9	96.5	94.0	+21.9	< 0.001	+34.7	< 0.001	
Testis <sup>2</sup>	73.8	88.4	86.1	88.4	86.1	88.5	+12.3	0.002	+ 0.1	0.031	
Kidney	61.5	69.4	65.9	78.2	75.5	81.9	+14.0	< 0.001	+12.5	< 0.001	
Bladder	66.3	72.1	70.8	75.9	75.1	74.2	+8.8	< 0.001	+2.1	0.255	
Brain and nervous system <sup>3</sup>	38.6	41.4	42.2	34.7	45.2	35.7	+ 6.5	0.002	-5.7	0.064	
Thyroid	80.1	89.4	87.3	91.9	94.2	97.6	+ 14.0	< 0.001	+8.2	< 0.001	
Hodgkin's lymphoma	81.6	68.7	82.4	81.2	83.8	87.4	+2.2	0.458	+18.8	< 0.001	
Non-Hodgkin's lymphoma	56.0	62.0	61.7	61.2	68.8	70.1	+12.8	< 0.001	+ 8.1	0.002	
Multiple myeloma	53.6	32.3	54.5	37.4	69.0	50.0	+15.4	< 0.001	+17.7	0.001	
Leukemia	54.4	61.3	51.5	60.2	64.4	64.0	+10.1	< 0.001	+2.7	0.053	

PE, period estimate; SE, standard error.

 $^{1}$ 15–59, 60–74 and 75+ age groups were used for age adjustment;  $^{2}$ 15–29, 30–44, 45+ age groups were used for age adjustment;  $^{3}$ 15–44, 45–59 and 60+ age groups were used for age adjustment;  $^{4}$ Percent units change in survival between 1995–1999 and 2005–2009.

than substantially better clinical outcomes. No mortality decline was seen for colorectal and breast cancer nor skin melanoma, although all three sites exhibited stronger rises in incidence than mortality, which allows for the interpretation of some moderate clinical progress. For both breast and colorectal cancer, further improvement in survival may be necessary before mortality declines, as seen in the western part of Europe for the last decades [12], will manifest in Lithuania. The increase in NHL case numbers reflects a steady rise in incidence in Lithuania until at least 2005 (Supplementary Figure 2 is available

Table IV. Number and proportion of patients by stage (of those with known stage) and age-adjusted 5-year relative survival of patients with colorectal, lung and breast cancer in Lithuania, 2005–2009.

Number and	d propo	rtion of	patients by	stage							
	Localized		Locally advanced		Regi	onal	Metastatic		Unknown		Total
	N	%	N	%	N	%	N	%	Ν	%	N
Colorectal	691	11.7	2110	35.6	1689	28.5	1433	24.2	1142	16.2	7065
Lung	526	10.7	378	7.7	1891	38.4	2132	43.3	1789	26.6	6716
Breast	2967	47.6	91	1.5	2610	41.9	565	9.1	800	11.4	7033
5-year perio	d estim	ates and	l standard ei	rrors by s	tage*.						
	Localized		Locally advanced		Regional		Metastatic		Unknown		
	PE	SE	PE	SE	PE	SE	PE	SE	PE	SE	
Colorectal	84.8	2.3	69.1	1.4	48.8	1.5	5.9	0.7	31.0	1.7	
Lung	37.1	2.5	7.1	1.3	5.9	0.7	0.8	0.2	6.7	0.9	
Breast	90.8	1.3	61.5	5.8	65.4	1.5	12.9	1.4	57.3	2.3	

N, number; PE, period estimate; SE, standard error.

\*for metastatic lung cancer, age adjustment was done using the age groups 15–59, 60–74 and 75+.

online at http//informahealthcare.com/doi/abs/ 10.3109/0284186X.2014.888495), which may be levelling off in the latest years. NHL incidence was found to rise throughout the second half of the 20th century [13], while more recently, increases were reported to attenuate in the US [14] and even decrease in some countries in Europe [13]. The consistent mortality declines were seen in Lithuania for HL and testicular cancer support clinical improvement in patient outcomes. Nevertheless, the low fiveyear survival for patients with testicular cancer for the 2005–2009 period is particularly concerning: both results of conditional survival analysis, indicating ongoing excess mortality beyond the first year after diagnosis, and the low survival comparison to European countries [15,16] clearly suggests inadequate availability of effective treatment for this patient population. Better access to effective therapies may be a persistent challenge in the Eastern part of Europe [17].

It is well known from comparative international cancer survival studies that there is major geographical variation in cancer survival in Europe [2,15, 18-21], with countries in Eastern Europe usually having substantially lower survival than most other countries in Northern and Western Europe. These geographic differences are mainly explained by access to or lack of latest diagnostic and treatment facilities, and the lack or lower use of prevention and screening programs [20]. Among the most common cancers with effective treatment options, despite the survival increase in the recent decade, five-year survival for colorectal and breast cancer, and also skin melanoma in 2005–2009 is still not exceeding the levels that were seen in 1990-1994 in Western and Northern European countries [15]. Differences are also seen for one-year survival, which in 2005-2009 was clearly below values seen in higher income countries in 2000-2007 [22]. With at least around a decade of time lag, the survival difference appears also meaningful for both HL [23] and NHL [15]. The survival of patients with cancers of usually very bad prognosis, such as liver, pancreas and lung cancer are similar to levels seen in other countries in Europe.

The 2005–2009 survival estimates seen for patients with prostate cancer in Lithuania are very high, and exceed levels seen for other European countries [15]. The very rapid rises in relative survival (+19% units between 1995–1999 and 2000–2004, and an additional +27% units by 2005–2009) are due to the lead time effect and overdiagnosis introduced by PSA testing in general, the effect of which has apparently strengthened after the introduction of the national PSA-based prostate cancer early detection program in 2006 [24]. With early diagnosis after PSA testing, the survival of patients

is artificially lengthened, even if the course of the disease is not changed. Overdiagnosis, i.e. the diagnosis of cancers that otherwise would not have been detected during the lifetime of the patient, additionally contributes to increasing survival. In the presence of these strong biases with PSA-based early detection [25], judgment on the extent of clinically relevant progress in survival becomes impossible.

In 2004 and 2005, early detection programs were started for cervical and breast cancers, respectively, and these programs may contribute to improving patient outcomes in the future. Further improving access to effective treatment, and ensuring that referral systems are in place to specialized treatment centers may help to improve outcomes among patients with rare diseases (i.e. testicular cancer), or cancer with evidence of better outcomes with centralization of care [26]. The monitoring of outcomes, as well as the effects of early detections programs is a key task of the cancer registry, and it is essential that registry operations receive adequate political, economic, juridical and medical support.

The quality of cancer registration and the completeness of follow-up could affect survival estimates. The percentage of death certificate only was 4.3%, and 95% of all common cancers diagnosed in the Lithuanian population during the study period could be included in this study, which generally suggests that the results can be expected to be of good general validity. Also, survival estimates found for low survival cancers suggest that the ascertainment of deaths is likely rather complete in general and survival estimates are not majorly affected by missing patient death information. At the same time, the substantial decrease seen in 5 1-year conditional survival of liver, lung, and brain and nervous cancer patients between 1995-1999 and 2000-2004 is potentially indicating better diagnostic work-up and improving registration quality among these patients, with the effect that fewer patients with metastatic disease from a different primary cancer being misclassified as having these primaries.

In conclusion, this first study of long-term trends in population-based cancer survival in Lithuania has found meaningfully increasing cancer survival for most forms of common cancers in the recent decade, but also persisting important gaps in cancer survival and major mortality trends between Lithuania and other European countries. Continued efforts will be necessary to ensure that resources available for health care are utilized in an effective way to reduce the persisting gaps in cancer survival. Maintaining and improving high quality cancer registration is essential for both monitoring of recently started screening programs for cervical, breast, prostate and colorectal cancer (2009), and cancer outcome research in general.

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#### Supplementary material available online

Supplementary Figure 1-5.

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