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TRENDS IN CANCER INCIDENCE AND MORTALITY – COMPARATIVE DATA WORLDWIDE, EUROPEAN UNION, AND ROMANIA

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Cancer is a worldwide major public health challenge, representing the second cause of death after cardiovascular diseases. In order to establish the proper ways of action, both in regard prevention and treatment, of their costs, and necessities for the infrastructure development, personnel forming and training, it is mandatory to know the very precise values of incidence and mortality by cancer. Using data coming from International Agency for Cancer Research (IARC) Lyon, France, there are analyzed and synthesized the values of these indicators for Romania, comparing to world and EU, for the principal 25 forms of malignancies; the analysis indicates continuous increases, for 2008–2012: for total, incidence grew with 12.03%, and mortality, with 4.21 %. The ratios between mortalities and incidences are, many times, higher than those in EU, and even worldwide, especially for colorectal, stomach, lip / oral cavity, thyroid, melanoma, larynx, and mainly – liver cancer. The specific situation of Romania imposes a stronger development of the prevention, of the uses of more performing treatment procedures, as well as, a more knowledge of the statistical data on cancer, and in this regard, it will be very necessary, to re-establish of the national cancer registry.

Keywords: cancer; incidence; mortality; cancer risk; cancer in Romania.

INTRODUCTION

Cancer is a worldwide major public health challenge, responsible for 25% of deaths, representing the second cause of death after cardiovascular diseases and the leading cause of death among people aged 45–64 years. A recent IARC (International Agency for Research on Cancer Lyon, France) report mentioned, in 2012, at worldwide level, a total of 14,068,000 new cases; the number of deaths was 8,202,000. In the European Union (EU), in the same year, the incidence was 2,612,000 and the mortality was 1,263,000[1,2]. In Romania, the incidence was 78,760 and mortality: 48,252. It estimates that for Europe, including Romania, the situation will become even more critical as European population is aging[3].

In all mentioned areas (globe / EU / Romania) it was observed a continuous increase both of the incidence and of the mortality by cancer, that are confirmed by relating the reported data for 2012 in respect to the previous ones, from 2008[4,5]. In 2008 there were reported, worldwide, a total of around 12,663,000 new cases and a value of death of 7,565,000. In the EU, the incidence in the same year was around 2,445,000 and mortality: 1,234,000, while in Romania the incidence was 70,300 and mortality: 46,300.

As a result of scientific progress, a more precise investigation of tissue particularities, of the cellular and molecular details of the disease, early detection in curable phases, and development, on this basis of more effective methods of treatment, curable of disease, we can appreciate that in the last years there were obtained encouraging results, demonstrated, among some others, by the evolution of ratio between mortality and incidence. However, if we refer to the absolute values of both incidence and mortality, which are growing, even in the developed countries, it is clear that sustainable efforts are still necessary in order to attend a stronger control of the disease and more significant positive results.

In this context, to identify the very specific ways of action for different forms of cancer, for infrastructure development, training and qualification of both physicians and other specialists, and not least, budgetary planning and health politics, both at global level, as well as, at the country level or even of a regions of a country,

there is necessary a very precise knowledge of the incidence and mortality values, data that usually represent the object of cancer registries.

Unfortunately, there are many problems related to the cancer statistics/registries; in this regard, we can mention:

• the existence of very different classification systems that were substantially changed over the time; first classifications were based on the location of the disease (topography), and only later there were added morphological details, situation that gave different interpretation when there are compared data obtained and processed at different time intervals. The classification variants that are currently in use: ICD-10[6] and ICD-O[7] are based on a double classification: topography / morphology, but there are significant differences between them, especially in terms of morphological details. In the recent years attempts were done in order to impose only the variant ICD-O (Revision 3), so we hope that in the future the data will be more consistent[8];

• classification difficulties – it is not uncommon that some forms of cancer to be considered into different categories: for example, lip cancer is part of "Malignant neoplasms of lip, oral cavity and pharynx" (C00 – C14), but if it is located on the surface of the lips (skin of lip) – detail that it is not always specified, it has to be included into the C43-C44 category of "Melanoma and other malignant neoplasms of skin (ICD-10)"[6,7,8];

• the existence, beside the malignant forms of cancer of the benign ones; the very precise certitude diagnosis is obtained only after identification of the cellular details that is achieved through specific investigations. From various reasons: not enough or even lack of biopsy material, investigation costs, lack of equipment or super-qualified personnel, similarly clinical manifestations, especially in debut, often it is not possible to achieve a clear distinction between the two forms; consequently the statistical data, sometimes only regionally, but sometime even at country level, include both forms of tumors as a single one and are reported as such[9];

• the need of a specialized infrastructure support to achieve a correct synthesis of cancer data and the elevated costs for carrying out these studies;

• lack of the data reporting;

• migration of people, extremely intense in recent years – situation that leads either to the absence of reports or to double reporting. A case that deserves to be mentioned is that of people from Romania with various forms of cancer that were migrated to Italy and are registered in regional registries of Italy: Parma and Turin regions[10];

• lack of reliable data on population from various countries or regions, both on the general population, and mainly on age-specificity ("standard population");

• in some countries there were issue of confidentiality of patient data that could justify such lack of reporting[9].

For these reasons, with few exceptions – small, but highly developed countries, there are not existing general data / national registries on cancer. This case is encountered even in some of the most developed economic countries such as Germany, Italy or France, that have only registries for certain regions of those countries[9]. For generalization, different statistical methods and mathematical functions were used[3]; however, the data, especially for incidence, exhibit an inaccurate character. Data on mortality are more reliable, because in this case there are used not only reports and statistics on cancer, but also the references of mortality, which are centralized by the WHO[11].

Romania, had, before 1990, a national registry, but later it has been replaced by eight regional registries (2007); it has to be mentioned that they were only partially done and only in some centers[12]. In these circumstances, beside some other necessary measures to achieve a stronger control of cancer, we appreciate that for Romania is more than useful to have a clear overview on the data regarding both the incidence and mortality by different forms of cancer at national level, based on the data coming from analysis done by specialized institution of WHO: International Agency for Research on Cancer in Lyon, France, analysis that covered the period 2008–2012.

DATA SOURCES. ANALYSIS METHODS

To attend the scope of the analysis – to emphasize the trends of cancer evolution, in Romania comparing to the world and EU, there were used the last data reported by IARC: EUCAN 2015[12], GLOBOCAN-2012[1], GLOBOCAN-2008[4], as well some critical analysis of the these data[2,5,13] – written acceptance from IARC to use both documents and papers was obtained. We have to mention that the reports were revised several times, the last one dating from 2015 (EUCAN 2015)[13]. Another mention regards the number of countries that were used for analysis on EU – now are 28 members, but because in 2012, as well as in 2008, there were only 27 – Croatia became EU member state only in 2013, we used the existing data on the rest 27 members, including Romania. In the analysis we made some considerations on the cancer situation at the world or EU levels, but attention was focused on trends of cancer in Romania. Data are synthesized in Tables 1–5.

Table 1

Cancer incidence (2012, absolute values)

Form of cancer	Total cases						Men						Women					
	World	Rank	**EU**	Rank	**Romania**	Rank	**World**	Rank	**EU**	Rank	**Romania**	Rank	**World**	Rank	**EU**	Rank	**Romania**	Rank
Total	14,067,894		2,612,332		78,760		7,410,376		1,417,495		43,149		6,657,518		1,194,837		35,611	
Lung, incl. trachea & bronchus	1,824,701	1	309,589	4	11,644	1	1,241,601	1	211,401	2	9,317	1	583,100	3	98,188	3	2,327	4
Breast	1,671,149	2	358,967	1	8,981	3							1,671,149	1	358,967	1	8,981	1
Colorectal	1,360,602	3	342,137	3	10,256	2	746,298	3	191,623	3	5,760	2	614,304	2	150,514	2	4,496	2
Prostate	1,094,916	4	343,174	2	4,532	4	1,094,916	2	343,174	1	4,532	3						
Stomach	951,594	5	80,626	8	4,075	6	631,293	4	49,933	6	2,711	5	320,301	5	30,693	10	1,364	8
Liver & intrahepatic bile duct	782,451	6	51,319	13	2,214	9	554,369	5	35,564	11	1,485	10	228,082	9	15,755	16	729	12
Cervix uteri	527,624	7	33,354	19	4,343	5							527,624	4	33,354	9	4,343	3
Esophagus	455,784	8	34,534	18	768	21	323,008	7	25,989	13	655	15	132,776	13	8,545	20	113	22
Bladder	429,793	9	123,135	5	3,825	7	330,380	6	96,442	4	3,151	4	99,413	19	26,693	13	674	14
Non-Hodgkin lymphomas	385,741	10	78,768	9	1,566	17	217,643	8	42,238	7	797	14	168,098	10	36,530	8	769	10
Leukemia	351,965	11	62,222	12	1,750	14	200,676	10	35,945	10	1,009	12	151,289	12	26,277	14	741	11
Pancreas	337,872	12	78,654	10	3,082	8	178,161	12	39,084	9	1,692	7	159,711	11	39,570	7	1,390	7
Kidney incl. renal pelvis & ureter	337,860	13	84,394	6	1,940	10	213,924	9	53,762	5	1,250	11	123,936	14	30,632	11	690	13
Corpus uteri	319,605	14	64,331	11	1,539	18							319,605	6	64,331	4	1,539	6
Lip & oral cavity	300,373	15	43,431	15	1,847	13	198,975	11	29,369	12	1,518	9	101,398	17	14,062	18	329	18
Thyroid	298,102	16	36,864	17	788	20	68,179	18	9,610	19	126	21	229,923	8	27,254	12	662	15
Brain & central nervous system	256,213	17	42,547	16	1,715	15	139,608	14	23,131	16	915	13	116,605	15	19,416	15	800	9
Ovary	238,719	18	44,149	14	1,850	12							238,719	7	44,149	5	1,850	5
Malignant melanoma of skin	232,130	19	82,075	7	1,121	19	120,649	16	39,571	8	528	16	111,481	16	42,504	6	593	16
Pharynx (all forms)	229,078	20	29,583	21	1,881	11	176,027	13	24,000	15	1,723	6	53,051	20	5,583	22	158	21
Gallbladder & biliary tract	178,101	21	23,546	23	632	23	76,844	17	9,607	20	261	19	101,257	18	13,939	19	371	17
Larynx	156,877	22	27,955	22	1,618	16	138,102	15	24,851	14	1,542	8	18,775	23	3,104	23	76	23
Multiple myeloma	114,251	23	33,413	20	644	22	62,469	19	17,935	18	323	18	51,782	21	15,478	17	321	19
Hodgkin lymphoma	65,950	24	12,271	25	318	25	38,520	21	6,655	21	135	20	27,430	22	5,616	21	183	20
Testis	55,266	25	18,008	24	340	24	55,266	20	18,008	17	340	17						
Other	1,111,177		173,286		5,491		603,468		89,603		3,379		507,709		83,683		2,112	
p% gender							52,68		54,26		54,79		47,32		45,74		45,21	
p% other forms	7,90		6,63		6,97		8,14		6,32		7,83		7,63		7,00		5,93	

Note: All the data from Tables 1–5 were extracted from documents: EUCAN 2015, GLOBOCAN 2012 coming from International Agency for Cancer Research Lyon, France (IARC). Written accept from IARC in order to use the documents was obtained.

Table 2

Cancer mortality (2012, absolute values)

Form of cancer	**Total cases**						**Men**						**Women**					
	World	Rank	**EU**	Rank	**Romania**	Rank	**World**	Rank	**EU**	Rank	**Romania**	Rank	**World**	Rank	**EU**	Rank	**Romania**	Rank
Total	8,201,575		1,262,976		48,252		4,653,385		707,755		28,875		3,548,190		555,221		19,377	
Lung, incl. trachea & bronchus	1,589,925	1	264,907	1	10,071	1	1,098,702	1	183,465	1	8,024	1	491,223	2	81,442	2	2,047	3
Breast	521,907	5	90,665	3	3,244	4							521,907	1	90,665	1	3,244	1
Colorectal	693,933	4	150,036	2	5,675	2	373,639	4	81,810	2	3,229	2	320,294	3	68,226	3	2,446	2
Prostate	307,481	8	71,033	5	2,018	7	307,481	5	71,033	3	2,018	4						
Stomach	723,073	3	57,699	6	3,366	3	468,970	3	34,914	5	2,217	3	254,103	5	22,785	6	1,149	6
Liver & intrahepatic bile duct	745,533	2	48,005	7	2,830	5	521,041	2	31,597	6	1,818	5	224,492	6	16,408	8	1,012	8
Cervix uteri	265,672	9	12,996	21	1,909	8							265,672	4	12,996	12	1,909	4
Esophagus	400,169	6	29,639	14	712	18	281,217	6	22,249	10	599	13	118,952	9	7,390	17	113	20
Bladder	165,084	13	40,268	9	1,471	10	123,051	9	29,922	7	1,180	7	42,033	17	10,346	14	291	14
Non-Hodgkin lymphomas	199,670	11	30,453	12	735	17	115,404	10	16,401	12	398	15	84,266	11	14,052	11	337	12
Leukemia	265,471	10	41,115	8	1,168	12	151,321	8	22,923	8	667	12	114,150	10	18,192	7	501	10
Pancreas	330,391	7	77,958	4	2,782	6	173,827	7	38,899	4	1,546	6	156,564	7	39,059	4	1,236	5
Kidney incl. renal pelvis & ureter	143,406	17	34,757	10	886	16	90,802	14	22,296	9	591	14	52,604	15	12,461	13	295	13
Corpus uteri	76,160	21	14,680	18	359	21							76,160	14	14,680	9	359	11
Lip & oral cavity	145,353	16	14,317	19	1,001	15	97,940	13	10,077	16	878	10	47,413	16	4,240	19	123	18
Thyroid	39,771	23	3,604	23	162	23	12,626	20	1,355	20	53	21	27,145	20	2,249	21	109	21
Brain & central nervous system	189,382	12	32,546	11	1,594	9	106,376	12	18,006	11	862	11	83,006	12	14,540	10	732	9
Ovary	151,917	14	29,770	13	1,020	13							151,917	8	29,770	5	1,020	7
Malignant melanoma of skin	55,488	22	15,724	17	364	20	31,390	18	8,807	17	189	17	24,098	21	6,917	18	175	16
Pharynx (all forms)	146,936	15	13,896	20	1,196	11	113,354	11	11,434	13	1,079	8	33,582	19	2,462	20	117	19
Gallbladder & biliary tract	142,823	18	15,989	16	466	19	60,339	16	6,139	18	201	16	82,484	13	9,850	16	265	15
Larynx	83,376	19	12,043	22	1,009	14	73,261	15	10,768	14	949	9	10,115	22	1,275	22	60	22
Multiple myeloma	80,019	20	20,322	15	344	22	43,091	17	10,387	15	176	18	36,928	18	9,935	15	168	17
Hodgkin lymphoma	25,469	24	2,673	24	116	24	15,463	19	1,529	19	61	20	10,006	23	1,144	23	55	23
Testis	10,351	25	909	25	63	25	10,351	21	909	21	63	19						
Other	702,815		136,972		3,691		383,739		72,835		2,077		319,076		64,137		1,614	
p% gender							56,74		56,04		59,84		43,26		43,96		40,16	
p% other forms	8,57		10,85		7,65		8,25		10,29		7,19		8,99		11,55		8,33	

Table 3

Cancer incidence (p% from total cases)

Form of cancer	**Total cases**						**Men**						**Women**					
	World	Rank	**EU**	Rank	**Romania**	Rank	**World**	Rank	**EU**	Rank	**Romania**	Rank	**World**	Rank	**EU**	Rank	**Romania**	Rank
Total	100.00		100.00		100.00		100.00		100.00		100.00		100.00		100.00		100.00	
Lung, incl. trachea & bronchus	12.97	1	11.85	4	14.78	1	16.75	1	14.91	2	21.59	1	8.76	3	8.22	3	6.53	4
Breast	11.88	2	13.74	1	11.40	3	0.00		0.00		0.00		25.10	1	30.04	1	25.22	1
Colorectal	9.67	3	13.10	3	13.02	2	10.07	3	13.52	3	13.35	2	9.23	2	12.60	2	12.63	2
Prostate	7.78	4	13.14	2	5.75	4	14.78	2	24.21	1	10.50	3	0.00		0.00		0.00	
Stomach	6.76	5	3.09	8	5.17	6	8.52	4	3.52	6	6.28	5	4.81	5	2.57	10	3.83	8
Liver & intrahepatic bile duct	5.56	6	1.96	13	2.81	9	7.48	5	2.51	11	3.44	10	3.43	9	1.32	16	2.05	12
Cervix uteri	3.75	7	1.28	19	5.51	5	0.00		0.00		0.00		7.93	4	2.79	9	12.20	3
Esophagus	3.24	8	1.32	18	0.98	21	4.36	7	1.83	13	1.52	15	1.99	13	0.72	20	0.32	22
Bladder	3.06	9	4.71	5	4.86	7	4.46	6	6.80	4	7.30	4	1.49	19	2.23	13	1.89	14
Non-Hodgkin lymphomas	2.74	10	3.02	9	1.99	17	2.94	8	2.98	7	1.85	14	2.52	10	3.06	8	2.16	10
Leukemia	2.50	11	2.38	12	2.22	14	2.71	10	2.54	10	2.34	12	2.27	12	2.20	14	2.08	11
Pancreas	2.40	12	3.01	10	3.91	8	2.40	12	2.76	9	3.92	7	2.40	11	3.31	7	3.90	7
Kidney incl. renal pelvis & ureter	2.40	13	3.23	6	2.46	10	2.89	9	3.79	5	2.90	11	1.86	14	2.56	11	1.94	13
Corpus uteri	2.27	14	2.46	11	1.95	18	0.00		0.00		0.00		4.80	6	5.38	4	4.32	6
Lip & oral cavity	2.14	15	1.66	15	2.35	13	2.69	11	2.07	12	3.52	9	1.52	17	1.18	18	0.92	18
Thyroid	2.12	16	1.41	17	1.00	20	0.92	18	0.68	19	0.29	21	3.45	8	2.28	12	1.86	15
Brain & central nervous system	1.82	17	1.63	16	2.18	15	1.88	14	1.63	16	2.12	13	1.75	15	1.62	15	2.25	9
Ovary	1.70	18	1.69	14	2.35	12	0.00		0.00		0.00		3.59	7	3.69	5	5.20	5
Malignant melanoma of skin	1.65	19	3.14	7	1.42	19	1.63	16	2.79	8	1.22	16	1.67	16	3.56	6	1.67	16
Pharynx (all forms)	1.63	20	1.13	21	2.39	11	2.38	13	1.69	15	3.99	6	0.80	20	0.47	22	0.44	21
Gallbladder & biliary tract	1.27	21	0.90	23	0.80	23	1.04	17	0.68	20	0.60	19	1.52	18	1.17	19	1.04	17
Larynx	1.12	22	1.07	22	2.05	16	1.86	15	1.75	14	3.57	8	0.28	23	0.26	23	0.21	23
Multiple myeloma	0.81	23	1.28	20	0.82	22	0.84	19	1.27	18	0.75	18	0.78	21	1.30	17	0.90	19
Hodgkin lymphoma	0.47	24	0.47	25	0.40	25	0.52	21	0.47	21	0.31	20	0.41	22	0.47	21	0.51	20
Testis	0.39	25	0.69	24	0.43	24	0.75	20	1.27	17	0.79	17	0.00		0.00		0.00	
Other	7.90		6.63		6.97		8.14		6.32				7.63		7.00		5.93	

Table 4

Cancer mortality (p% from total cases)

Form of cancer	Total cases						Men						Women					
	World	Rank	**EU**	Rank	**Romania**	Rank	**World**	Rank	**EU**	Rank	**Romania**	Rank	**World**	Rank	**EU**	Rank	**Romania**	Rank
Total	100.00		100.00		100.00		100.00		100.00		100.00		100.00		100.00		100.00	
Lung, incl. trachea & bronchus	19.39	1	20.97	1	20.87	1	23.61	1	25.92	1	27.79	1	13.84	2	14.67	2	10.56	3
Breast	6.36	5	7.18	3	6.72	4	0.00		0.00		0.00		14.71	1	16.33	1	16.74	1
Colorectal	8.46	4	11.88	2	11.76	2	8.03	4	11.56	2	11.18	2	9.03	3	12.29	3	12.62	2
Prostate	3.75	8	5.62	5	4.18	7	6.61	5	10.04	3	6.99	4	0.00		0.00		0.00	
Stomach	8.82	3	4.57	6	6.98	3	10.08	3	4.93	5	7.68	3	7.16	5	4.10	6	5.93	6
Liver & intrahepatic bile duct	9.09	2	3.80	7	5.87	5	11.20	2	4.46	6	6.30	5	6.33	6	2.96	8	5.22	8
Cervix uteri	3.24	9	1.03	21	3.96	8	0.00		0.00		0.00		7.49	4	2.34	12	9.85	4
Esophagus	4.88	6	2.35	14	1.48	18	6.04	6	3.14	10	2.07	13	3.35	9	1.33	17	0.58	20
Bladder	2.01	13	3.19	9	3.05	10	2.64	9	4.23	7	4.09	7	1.18	17	1.86	14	1.50	14
Non-Hodgkin lymphomas	2.43	11	2.41	12	1.52	17	2.48	10	2.32	12	1.38	15	2.37	11	2.53	11	1.74	12
Leukemia	3.24	10	3.26	8	2.42	12	3.25	8	3.24	8	2.31	12	3.22	10	3.28	7	2.59	10
Pancreas	4.03	7	6.17	4	5.77	6	3.74	7	5.50	4	5.35	6	4.41	7	7.03	4	6.38	5
Kidney incl. renal pelvis & ureter	1.75	17	2.75	10	1.84	16	1.95	14	3.15	9	2.05	14	1.48	15	2.24	13	1.52	13
Corpus uteri	0.93	21	1.16	18	0.74	21	0.00		0.00		0.00		2.15	14	2.64	9	1.85	11
Lip & oral cavity	1.77	16	1.13	19	2.07	15	2.10	13	1.42	16	3.04	10	1.34	16	0.76	19	0.63	18
Thyroid	0.48	23	0.29	23	0.34	23	0.27	20	0.19	20	0.18	21	0.77	20	0.41	21	0.56	21
Brain & central nervous system	2.31	12	2.58	11	3.30	9	2.29	12	2.54	11	2.99	11	2.34	12	2.62	10	3.78	9
Ovary	1.85	14	2.36	13	2.11	13	0.00		0.00		0.00		4.28	8	5.36	5	5.26	7
Malignant melanoma of skin	0.68	22	1.24	17	0.75	20	0.67	18	1.24	17	0.65	17	0.68	21	1.25	18	0.90	16
Pharynx (all forms)	1.79	15	1.10	20	2.48	11	2.44	11	1.62	13	3.74	8	0.95	19	0.44	20	0.60	19
Gallbladder & biliary tract	1.74	18	1.27	16	0.97	19	1.30	16	0.87	18	0.70	16	2.32	13	1.77	16	1.37	15
Larynx	1.02	19	0.95	22	2.09	14	1.57	15	1.52	14	3.29	9	0.29	22	0.23	22	0.31	22
Multiple myeloma	0.98	20	1.61	15	0.71	22	0.93	17	1.47	15	0.61	18	1.04	18	1.79	15	0.87	17
Hodgkin lymphoma	0.31	24	0.21	24	0.24	24	0.33	19	0.22	19	0.21	20	0.28	23	0.21	23	0.28	23
Testis	0.13	25	0.07	25	0.13	25	0.22	21	0.13	21	0.22	19	0.00		0.00		0.00	
Other	8.57		10.85		7.65		8.25		10.29		7.19		8.99		11.55		8.33	

Table 5

Ratios between mortality and incidence (p%)

Form of cancer	Total cases						Men						Women					
	World	Rank	**EU**	Rank	**Romania**	Rank	**World**	Rank	**EU**	Rank	**Romania**	Rank	**World**	Rank	**EU**	Rank	**Romania**	Rank
Total	58.30		48.35		61.26		62.80		49.93		66.92		53.30		46.47		54.41	
Lung, incl. trachea & bronchus	87.13	4	85.57	4	86.49	5	88.49	3	86.79	3	86.12	5	84.24	4	82.94	4	87.97	5
Breast	31.23	20	25.26	19	36.12	21							31.23	20	25.26	19	36.12	19
Colorectal	51.00	14	43.85	12	55.33	11	50.07	13	42.69	12	56.06	12	52.14	13	45.33	11	54.40	12
Prostate	28.08	21	20.70	22	44.53	17	28.08	18	20.70	19	44.53	17						
Stomach	75.99	6	71.56	6	82.60	6	74.29	8	69.92	6	81.78	6	79.33	6	74.24	6	84.24	6
Liver & intrahepatic bile duct	95.28	2	93.54	2	127.82	1	93.99	2	88.85	2	122.42	1	98.43	1	104.14	1	138.82	1
Cervix uteri	50.35	15	38.96	16	43.96	18							50.35	14	38.96	15	43.96	14
Esophagus	87.80	3	85.83	3	92.71	3	87.06	4	85.61	4	91.45	3	89.59	3	86.48	3	100.00	2
Bladder	38.41	19	32.70	18	38.46	19	37.25	17	31.03	16	37.45	19	42.28	18	38.76	16	43.18	16
Non-Hodgkin lymphomas	51.76	13	38.66	15	46.93	15	53.02	12	38.83	14	49.94	14	50.13	15	38.47	17	43.82	15
Leukemia	75.43	7	66.08	9	66.74	8	75.41	7	63.77	8	66.11	8	75.45	7	69.23	7	67.61	10
Pancreas	97.79	1	99.12	1	90.27	4	97.57	1	99.53	1	91.37	4	98.03	2	98.71	2	88.92	4
Kidney incl. renal pelvis & ureter	42.45	17	41.18	14	45.67	15	42.45	15	41.47	13	47.28	15	42.44	17	40.68	14	42.75	17
Corpus uteri	23.83	23	22.82	20	23.33	23							23.83	21	22.82	20	23.33	22
Lip & oral cavity	48.39	16	32.96	17	54.20	13	49.22	14	34.31	15	57.84	11	46.76	16	30.15	18	37.39	18
Thyroid	13.34	25	9.78	24	20.56	24	18.52	20	14.10	20	42.06	18	11.81	23	8.25	23	16.47	23
Brain & central nervous system	73.92	8	76.49	5	92.94	2	76.20	6	77.84	5	94.21	2	71.19	9	74.89	5	91.50	3
Ovary	63.64	11	67.43	8	55.14	12							63.64	10	67.43	9	55.14	11
Malignant melanoma of skin	23.90	22	19.16	23	32.47	22	26.02	19	22.26	18	35.80	20	21.62	22	16.27	22	29.51	21
Pharynx (all forms)	64.14	10	46.97	11	63.58	9	64.40	10	47.64	10	62.62	9	63.30	11	44.10	12	74.05	8
Gallbladder & biliary tract	80.19	5	67.91	7	73.73	7	78.52	5	63.90	7	77.01	7	81.46	5	70.67	7	71.43	9
Larynx	53.15	12	43.08	13	62.36	10	53.05	11	43.33	11	61.54	10	53.87	12	41.08	13	78.95	7
Multiple myeloma	70.04	9	60.82	10	53.42	14	68.98	9	57.91	9	54.49	13	71.31	8	64.19	10	52.34	13
Hodgkin lymphoma	38.62	18	21.78	21	36.48	20	40.14	16	22.98	17	45.19	16	36.48	19	20.37	21	30.05	20
Testis	18.73	24	5.05	25	18.53	26	18.73	21	5.05	21	18.53	21						
Other	63.25		79.04		67.22		63.59		81.29		61.47		62.85		76.64		76.42	

Tables 1 and 2 show the absolute numerical values of incidence, respectively, of cancer mortality in 2012, worldwide, the European Union, and Romania, respectively.

To have a clearer image on the rank of diverse forms of cancer and on their significance in each area, percentages for each form were calculated using the absolute values for incidence and mortality, respectively, in respect to the total values for each area – results are presented in Tables 3 and 4.

In order to identify the more aggressive malignancies – cancers with high values of mortality, in contrast to some more „gentle" ones, we made another calculus: ratio (as percentages) between mortality and incidence for every form of cancer and every area; results are presented in Table 5.

In order to have an easier interpretation of the values, all the tables contain rank stratifications of the data.

RESULTS

The data extracted from mentioned reports shows that, worldwide, only for the period 2008–2012, the number of new cases increased by over 1,405,000 or 11.10%. The mortality had an absolute increase of 637,000 deaths, which correspond to an 8.41% increase. It can be observed a lower increase of mortality, which can be attributed among others, to early stages of detection, extension uses of more efficient treatment methods, with more positive responses.

In the EU, variations were:

• Incidence: +167,000 (+ 6.83%);

• Mortality: +29,000 (+ 2.35%).

For Romania increases were:

• Incidence: +8,460 (+ 12.03%);

• Mortality: +1,952 (+ 4.21%).

Although all organs of the body could be affected, some cancer locations can be considered as "major" – we appreciate that could be included in this category malignancies with more than 50,000 new cases/year, all over the world, or more than 0.4% from the total new cases (in 2012).

Data relating to various cancers are presented and analyzed in the next chapter.

DISCUSSIONS

Problem of cancer disease is extremely complex, that are generated by the existence, in fact, of over 200 different forms (and according to the latest estimates, which take into account the molecular-genetic details of the disease, the actual number might be over a thousand), with events, evolution and, of course, with specific treatment methods[14,15]. There are used different methods of classification for various forms of cancer, but the most common is the location that are correspondently coded: malignant neoplasms of lip, oral cavity and pharynx (code C00-C14), neoplasms of digestive organs (C15-C26), respiratory and intrathoracic organs (C30-C39), breast (C50), genital organs, etc. (ICD-10, ICD-O)[6,7], every category having several sub-categories. From the different forms of cancers, we may consider 25 cancers to be majors ones, which account for over 92% of the total, all other locations give only around 8%. We have to mention that some cancers are found only in one of the two genders: testicle and prostate cancers in men, cancers of the breast, ovary and uterus in women, respectively; to note that actually, there are forms of breast cancer in men, but the percentage is very small, less than 1% of the total, most often they are not mentioned in statistics, although they are more aggressive comparing to women.

Worldwide, the *incidences* values for the main forms cancers were, for 2012 (p% from total cases): lung (12.97%) > breast (11.88%) > colorectal (9.67%) > prostate (7.78%) > stomach (6.76%) > liver (5.56%) > cervix (3.75%) > esophagus (3.24%) > bladder (3.05%) > non-Hodgkin's lymphoma (2.74%) (Tables 1, 3). By gender, obviously, the order is different: in men, predominates lung cancer (16.75%) and prostate (14.78%), followed by colorectal (10.07%), stomach (8.52%) and liver (7.48%), and for women, breast cancer is the most present, with more than 1/4 of the total number of cases, followed by colorectal (9.23%) and lung (8.76%); high values are recorded in regards "genital", cancer, particularly, the cervix (7.93%).

The recorded values for *mortality* lead to an order somewhat different from that on the incidence (Tables 2, 4). At total cases, the first place continues to be lung cancer, but with much higher percentage values in relation to incidence: 19.39%, followed by liver (9.09%), stomach (8.82%), colorectal (8.46%) and breast (6.36%). By gender, the main cancers with high mortality for men are: lung cancer (23.61%), liver (11.20%), and stomach (10.08%), colorectal (8.03%), and

prostate (6.61%), while for the women order is: breast cancer (14.71%), lung (13.84%), colorectal (9.03%), cervix (7.49%), and stomach (7.16%).

From the data presented in Table 5 (percentage of mortality versus incidence), it may be noticed the existence of very aggressive forms of cancers, with the mortality values very close to those of incidence. In this regards, for total cases, we can mention: pancreatic cancer (97.79%), liver (95.28%), esophagus (87.80%), lung (87.13%), and gallbladder (80.19%). In contrast, more "gentle" cancers may be considered: thyroid (13.34%), testis (18.73%), uterus (23.83%), melanoma (skin) (23.90%), prostate (28.08%). In men, the most aggressive forms are: pancreatic cancer (97.57%), liver (93.99%), lung (88.49%), esophagus (87.06%), gallbladder (78.52%), and "gentle": thyroid (18.52%), testicle (18.73%), melanoma (26.02%) and prostate (28.08%). In women, very aggressive are: liver cancer (98.43%), pancreas (98.03%), esophagus (89.59%), lung (84.24%), and gallbladder (81.46%) and less aggressive: thyroid (11.81%), melanoma (21.62%), uterus (23.83%) and even breast (31.23%).

EU

At EU level, in 2012, as *incidence*, breast cancer, with 13.74% from total, is on the first place, followed by prostate (13.14%) and colorectal (13.10%). Lung cancer is only on fourth place (11.85%) – probably as the result of a decrease of smoking. We have to observe that these four forms represent, together, more than 50% of total. Elevated values there were registered for bladder (4.71%) > kidney (3.23%) > melanoma (3.14%) > stomach (3.09%) > non-Hodgkin lymphoma (3.02%) > pancreas (3.01%), and reduced ones, for: Hodgkin lymphoma (0.47%) < testis (0.69%) < gallbladder (0.90%) < larynx (1.07%). At men, very high incidence is observed for prostate – near 25% (24.21%), followed by: lung (14.91%) > colorectal (13.52%) > bladder (6.80%) > kidney (3.79%), reduced values are observed for: Hodgkin lymphoma (0.47%) < gallbladder (0.68%) < thyroid (0.68%) < multiple myeloma (1.27%). At women, breast cancer represents more than 30% from the total, followed by colorectal (12.60%) > lung (8.22%) > corpus uteri (5.38%) > ovary (3.69%), the lowest values being: larynx (0.26%) < pharynx (0.47%) < Hodgkin lymphoma (0.47%).

At *mortality*, to both genders, order is: lung (20.97%) > colorectal (11.88%) > breast (7.18%) > pancreas (6.17%) > stomach (4.93%). At men, lung cancer overpasses 25% (25.92%), than come: colorectal (11.56%) > prostate (10.04%) > pancreas (5.50%) > stomach (4.93%) > liver (4.46%), and at women, the principal forms are: breast (16.33%) > lung (14.67%) > colorectal (12.29%) > pancreas (7.03%) > ovary (5.36%) > stomach (4.10%).

From the data presented in Table 5, referring to ratio between mortality and incidence, result that the most aggressive are, at total: pancreas (99.12%) > liver (93.54%) > esophagus (85.83%) > lung (85.57%) > brain / central nervous system (76.49%) > stomach (71.56%), less aggressive being: testis (5.05%) < thyroid (9.78%) < melanoma (19.16%) < prostate (20.70%) – order very similar to that on the world. At men, aggressive forms are: pancreas (99.53%) > liver (88.85%) > lung (86.79%) > esophagus (85.61%) > brain (77.84%) > stomach (69.92%), and less aggressive (again similar to the world): testis (5.05%) < thyroid (14.10%) < prostate (20.70%). At women, order is: liver (104.14%) > pancreas (98.71%) > esofagus (86.48%) > lung (82.94%) > brain (74.89%), lower values are for: thyroid (8.25%) < melanoma (16.27%) < Hodgkin lymphoma (20.37%) < breast (25.26%).

Romania

Incidence. In 2012, for both genders (total), the situation for major forms is somewhat different from the world or the EU; first is lung cancer (14.78%), followed by colorectal cancer (13.02%), breast cancer (11.40%) and prostate (5.75%); higher values are observed in cervix (5.51%), stomach (5.17%), bladder (4.86%), pancreas (3.91%) cancers. Lower values are observed for: Hodgkin lymphoma (0.40%), testis (0.43%), gallbladder (0.80%), multiple myeloma (0.82%), esophageal cancer (0.98%) and thyroid (1.00%).

In men, the order of the main forms is: lung cancer (21.59%) > colorectal (13.35%) > prostate (10.50%) > bladder (7.30%) > stomach (6.28%) > pharynx (3.99%) > pancreas (3.92%) > kidney (3.75%) > larynx (3.57%) > lip / oral cavity (3.52%) > liver (3.44%) and in women sequence is: breast cancer (25.22%) > colorectal (12.63%) > cervix (12.20%) > lung (6.53%) > ovary (5.20%) > uterus (4.32%) > pancreas (3.90%) > stomach (3.83%).

Mortality. Percentage values of mortality, for total cases are close, in many cases, to those recorded in the EU: lung cancer: 20.87% (Romania) / 20.97% (EU); colorectal: 11.76% / 11.88%; breast cancer: 6.72% / 7.18%; pancreas: 5.77% / 6.17%; bladder: 3.05% / 3.19%, but there are some significant differences: liver: 5.87% / 3.80%; stomach: 6.98% / 4.57%; cervix: 3.96% / 1.03%. In relation to worldwide situation, in Romania, but similar to EU, it has to be mentioned the existence of elevated values of death for colorectal cancers (ranks: world: 4 / EU: 2 / Romania: 2) and lower values for liver (ranks: 2 / 7 / 5).

In men, the order is: lung (27.79%) – by far, the location with the highest percentages of death by cancer > colorectal (11.18%) > stomach (7.68%) > prostate (6.99%) > liver (6.30%) > pancreas (5.35%) > bladder (4.09%). In relation to the world, the differences are quite often significant: liver (rank 2), esophagus (6), pancreas (7), being close to those registered in the EU: EU/Romania ranks (same forms): 6/5; 10/13; 4/6. In regards to EU, there are differences in terms of stomach cancer (EU/Romania ranks: 5/3, lips / oral cavity (16/10), larynx (14/9) (higher values in Romania), and contrary to EU: prostate cancer (3/4), multiple myeloma (15/18), with lower values.

Many similarities with EU are observed for females, too: breast cancer: 16.74% Romania / 16.33% EU colorectal: 12.62% / 12.29%; ovary: 5.26% / 5.36%, gallbladder: 1.37% / 1.77%. There are also a few cases with significant positive differences: lung – lower values for Romania comparing to EU (10.56% / 14.67%), probably due to a still lower extension of smoking in women, and multiple myeloma: 0.87% / 1.79%. Contrary, there are some forms with negative differences: stomach cancer: 5.93% / 4.10%; liver: 5.22% / 2.96% and, especially, cervical cancer: 9.85% / 2.34%, in the last case, the value is even higher than the world average (7.49%).

Mortality / incidence ratio. The ratio between the mortality and the incidence is probably the most significant illustration of the cancer situation in Romania compared to the EU or global levels, particularly in terms of early detection or the efficiency of treatments (Table 5).

Similarly to the situations referred worldwide or EU, there are some forms of cancers that are very aggressive, with mortality values very close to those of incidence: lung, pancreas, liver, esophagus, brain / nervous system. Unfortunately, for Romania, many values of mortality / incidence reports are much higher in regards to EU and even at global level. Thus, the total cases values (in percent) are (in order of Romania / EU / world): colorectal: 55.33% / 43.85% / 51.00%; stomach: 82.60% / 71.56% / 75.99; lip / oral cavity: 54.20% / 32.96% / 48.39%; thyroid: 20.56% / 9.78% / 13.34%, melanoma: 32.47% / 19.16% / 23.90%; larynx: 62.36% / 43.08% / 53.15%. The situation is more dramatic in liver cancer: 127.82% / 93.54% / 95.28%, the number of deaths for the year under review (2012) exceeded the number of new cases that had occurred! A much higher proportion of deaths in relation to incidence are confirmed by the overall mean value for all cancers: 61.26% (Romania) / 48.35% (EU) / 58.30% (globe).

The negative situation mentioned for both sexes is found, obviously, when we analyze the situation for each sex separately. In men, the values for total cancers are (Romania / EU / world): 66.92% / 49.93% / 62.80%. For different location, beside the liver cancer (122.42% / 88.85% / 93.99%) it can be mentioned: prostate cancer: 44.53% / 20.70% / 28.08%; testicle: 18.53% / 5.05% / 18.73%; thyroid: 42.06% / 14.10% / 18.52%; Hodgkin lymphoma: 45.19% / 22.98% / 40.14%, all with significant, negative, differences compared to the EU and even the world. It has to be mentioned that are some cancers with better values and lower differences: colorectal, stomach, non-Hodgkin lymphoma, lip / oral cavity, brain / nervous system, melanoma, pharynx, gallbladder, larynx. Although at female gender the values are often negative, especially comparing to the EU values, the differences seem to be somewhat less significant. At total, the values are: 54.41% / 46.47% / 53.30%, and the location, most significant are: liver cancer: 138.82% / 104.14% / 98.43%; thyroid: 16.47% / 8.25% / 11.81%; brain / nervous system: 91.50% / 74.89% / 71.19%; melanoma: 29.51% / 16.27% / 21.62%; Hodgkin lymphoma: 30.05% / 20.37% / 36.48%, but with large differences for other two locations; pharynx: 74.05% / 44.10% / 63.30% and larynx: 78.95% / 41.08% / 53.87%.

A special analysis deserves the breast cancer – it is, by far, the most common form of cancer in women. Worldwide, in 2012, there were 1,671,149 new cases (25.10% of total), at EU level: 358,967 (30.04%), and in Romania: 8,981 cases (25.22%). In respect to the total, the mortality values are much lower: the world: 521,907 (14.71% of total cancer deaths), EU: 90,665 (16.33%) and for

Romania 3,244 (16.74%). Thereby, the ratios between the deaths and incidences are lower; worldwide: 31.23%, EU: 25.26% Romania: 36.12% (it can again observed the higher values in Romania), so less than 1/3 of cases lead to death, the values being among the lowest comparing to other forms of malignancies. We consider that this situation is very significant that is the result of strong efforts made in all areas:

• early detection – many countries have introduced mammography as a general test at population over 45 years. Especially in the recent years, investigations at the genetic level, mainly for BRCA genes were done, too;

• development of scientific studies devoted to (i) mechanisms of appearance, and evolution of the disease; (ii) identification of risk factors (some even with regional action) and (iii) going on with a detailed molecular and genetic particularities – based on such details specific drugs were developed and produced (*e.g.* Herceptin);

• development of all forms of treatment: surgery, radio-, chemo- and hormone therapy;

• monitoring of the patients evolution, for long periods of time, that included determinations of some tumor markers that predict the evolution to metastasis;

• use of post-therapy forms: administration of tamoxifen, and more recently, of aromatase inhibitors.

As consequence of these multiple way of action, best results in breast cancer became possible, even for advanced forms (stage IV, metastatic), very remarkable results being obtained in early forms (0 / I) when the positives responses exceed 90%.

Mentioned results obtained in breast cancer are undoubtedly encouraging, but the same efforts should be made for other forms of cancer, where the results are still far from expectations: lung, liver, stomach, pancreas, colorectal and many others.

From the data referring to EU, it can easily see that growth rates, both for incidence and mortality are significantly lower than the world average. Majority of EU countries could be included into the category of ”developed” ones, which is manifested not only at the economic or social levels, but also through the actions done in public health. Beyond expanding preventive measures, new treatment methods and new drugs have been developed. The results of these efforts are highlighted, especially, by the much lower values of increasing rates of cancer mortality. Apparently, these results seem spectacular, and they represent the results of efforts at all levels, primarily, intelligence and research, and, not at the least, of financial nature. *But! However, there is a "but"; if we are looking to the figures of cancer incidence and mortality, even at EU level (1,263,000 deaths in 2012), and mainly at the world (8,200,000), they continue to be enormous: the number of deaths worldwide corresponds to population of average country, and to the EU level, to those of a city with over 1,000,000 inhabitants. It is clear that still are needed further special efforts to control of the disease, to arrive to a moment when the variation slopes for incidence and, in particular, for mortality, will achieved negative values.*

In this scope, certainly, there are many possibilities, but we consider the most important to be:

• prevention – an area with many development directions, including genetic / familial details, but also, environmental carcinogens identification and their control;

• intensively development of the studies that detail the molecular-genetic profile of the disease, and, if possible, control of the changes, sometimes very insidious and restricted (such as simple substitution of one nucleotide in the DNA structure) which lead to the transformation of normal cells in cancer cells and, later, to metastatic form, most difficult, if not impossible to control!

Of course, these efforts must be attended in any country in the world, but for some countries, these efforts must be more intensive. Romania is one of these countries – it is evident from the data that were reported in this analysis that the ratios between the mortality and the incidence for many forms of cancer are very often superior not only to the values on EU, but to even to those observed at worldwide level. Certainly, in Romania there were made great financial efforts, with increasingly funds coming both from national programs and National Health Insurance House. But if we look to the values specified above for the growth rates in the period 2008–2012, the incidence (+12.03%), respectively, of cancer mortality (+4.21%) are significant higher to EU: +6.83% for incidence, and +2.35% – for mortality. Comparing to the world (incidence growth: +11.10%, mortality +8.41%), incidence value for Romania is still higher, but instead – and this is a great result, increasing mortality rate is approx. 1/2 of the world!

Finally, we can conclude that, for Romania there are existing positive results for some forms of cancer, demonstrated by lower values / increases of mortalities, comparing to incidence. But the general values referring to incidence and mortality, as well as the ratios values between mortality and incidence, that are many times more elevated than EU or even world, give mandatory obligations, not only for physicians and researchers, but also for the entire population, and mainly for the decision and coordination institutions / politicians, in order to identify, to promote and to use of the newest methods and mechanisms of cancer control, mainly in regards a real prevention, based on the latest knowledge on molecular and genetic particularities of cancer. *In this respect, very important, in order to have very precise data on cancer, both for total, and specific localizations, we appreciate, that there is more than necessary, to re-establish the national cancer registry.*

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